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L65 ANSWER 1 OF 49 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:850136 HCAPLUS
DN 137:358064
TI Stem cells of the **islets** of **Langerhans** and their use
in treating diabetes mellitus
IN Habener, Joel F.; Zulewski, Henryk; Thomas, Melissa K.; Abraham, Elizabeth
J.; Vallejo, Mario; Leech, Colin A.
PA USA
SO U.S. Pat. Appl. Publ., 51 pp., Cont.-in-part of U. S. Ser. No. 731,261.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K048-00
NCL 424093700
CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 2, 9, 15
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002164307	A1	20021107	US 2001-963875	20010926 <--
	US 2001046489	A1	20011129	US 2000-731261	20001206 <--
PRAI	US 1999-169082P	P	19991206	<--	
	US 2000-215109P	P	20000628		
	US 2000-238880P	P	20001006		
	US 2000-731261	A2	20001206		
AB	Methods and compns. are described for the treatment of type I insulin -dependent diabetes mellitus and other conditions using newly identified stem cells that are capable of differentiation into a variety of pancreatic islet cells, including insulin -producing beta cells, as well as hepatocytes. Nestin and the GLP-1 receptor have been identified as mol. markers for pancreatic stem cells, while cytokeratin-19 serves as a marker for a distinct class of islet ductal cells. Methods are described whereby stem cells which express one or both				

of nestin and GLP-1R can be isolated from pancreatic islets and cultured to obtain further stem cells or pseudo-islet like structures. Methods for ex vivo differentiation of the pancreatic stem cells are disclosed. Methods are described whereby pancreatic stem cells can be isolated, expanded, and **transplanted** into a patient in need thereof, either allogeneically, isogeneically or xenogenically, to provide replacement for lost or damaged **insulin**-secreting cells or other cells.

- ST stem cell **islet Langerhans** isolation nestin GLP1R diabetes
- IT Antibodies
 - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (GAD65; stem cells of the **islets** of **Langerhans** and their use in treating diabetes mellitus)
- IT Transcription factors
 - RL: PAC (Pharmacological activity); BIOL (Biological study)
 - (IDX-1; stem cells of the **islets** of **Langerhans** and their use in treating diabetes mellitus)
- IT Liver
 - (hepatocyte, formation of; stem cells of the **islets** of **Langerhans** and their use in treating diabetes mellitus)
- IT Proteins
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (nestins, stem cell marker, amino acid sequence of; stem cells of the **islets** of **Langerhans** and their use in treating diabetes mellitus)
- IT Cell differentiation
 - (of **insulin**-producing cells; stem cells of the **islets** of **Langerhans** and their use in treating diabetes mellitus)
- IT Glucagon-like peptide-1 receptors
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (stem cell marker; stem cells of the **islets** of **Langerhans** and their use in treating diabetes mellitus)
- IT Animal tissue culture
 - Antidiabetic agents
 - Diabetes mellitus
 - Endoscopes
 - Immunosuppressants
 - Molecular cloning
 - Pancreatic islet of Langerhans**
 - Protein sequences
 - Transplant and Transplantation**
 - cDNA sequences
 - (stem cells of the **islets** of **Langerhans** and their use in treating diabetes mellitus)
- IT Hepatocyte growth factor
 - RL: PAC (Pharmacological activity); BIOL (Biological study)
 - (stem cells of the **islets** of **Langerhans** and their use in treating diabetes mellitus)
- IT Cell
 - (stem, neural; stem cells of the **islets** of **Langerhans** and their use in treating diabetes mellitus)
- IT Collagens, biological studies
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (type IV, antibodies specific for; stem cells of the **islets** of **Langerhans** and their use in treating diabetes mellitus)
- IT **Pancreatic islet of Langerhans**
 - (.alpha.-cell; stem cells of the **islets** of **Langerhans** and their use in treating diabetes mellitus)
- IT Transforming growth factors
 - RL: PAC (Pharmacological activity); BIOL (Biological study)
 - (.beta.-; stem cells of the **islets** of **Langerhans**)

and their use in treating diabetes mellitus)

IT **Pancreatic islet of Langerhans**
 (.beta.-cell; stem cells of the **islets** of
Langerhans and their use in treating diabetes mellitus)

IT **9004-10-8, Insulin**, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (formation of; stem cells of the **islets** of **Langerhans**
 and their use in treating diabetes mellitus)

IT 11028-71-0, Concanavalin a
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (stem cells of the **islets** of **Langerhans** and their
 use in treating diabetes mellitus)

IT 50-99-7, Glucose, biological studies 62229-50-9, Egf 89750-14-1,
 Glucagon-like peptide I 104625-48-1, Activin a **106096-93-9**,
 Fibroblast growth factor 2 141732-76-5, Exendin 4 148348-15-6,
 Fibroblast growth factor 7 163150-12-7, Betacellulin
 RL: PAC (Pharmacological activity); BIOL (Biological study)
 (stem cells of the **islets** of **Langerhans** and their
 use in treating diabetes mellitus)

IT 79217-60-0, Cyclosporin 104987-11-3, Fk506
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (stem cells of the **islets** of **Langerhans** and their
 use in treating diabetes mellitus)

IT 474865-30-0 474865-31-1 474865-32-2 474865-33-3 474865-34-4
 474865-35-5 474865-36-6 474865-37-7 474865-38-8 474865-39-9
 474865-40-2 474865-41-3 474865-42-4 474865-43-5 474865-44-6
 474865-45-7 474865-46-8 474865-47-9 474865-48-0 474865-49-1
 474865-50-4 474865-51-5 474865-52-6 474865-53-7 474865-54-8
 474865-55-9 474865-56-0 474865-57-1 474865-58-2 474865-59-3
 474865-60-6 474865-61-7 474865-62-8 474865-63-9 474865-64-0
 474865-65-1 474865-66-2 474865-67-3 474865-68-4 474865-69-5
 474865-70-8 474865-71-9 474865-72-0 474865-73-1 474865-74-2
 474865-75-3 474865-76-4 474865-77-5 474865-78-6 474865-79-7
 474865-80-0 474865-81-1 474865-82-2 474865-83-3 474865-86-6
 RL: PRP (Properties)
 (unclaimed nucleotide sequence; stem cells of the **islets** of
Langerhans and their use in treating diabetes mellitus)

IT 474865-87-7
 RL: PRP (Properties)
 (unclaimed protein sequence; stem cells of the **islets** of
Langerhans and their use in treating diabetes mellitus)

IT 474865-84-4 474865-85-5
 RL: PRP (Properties)
 (unclaimed sequence; stem cells of the **islets** of
Langerhans and their use in treating diabetes mellitus)

L65 ANSWER 2 OF 49 HCAPLUS COPYRIGHT 2002 ACS
 AN 2001:798040 HCAPLUS
 DN 135:339222
 TI Inhibition of abnormal cell proliferation with camptothecin or a
 derivative, analog, metabolite, or prodrug thereof, and combinations
 including camptothecin
 IN Rubinfeld, Joseph
 PA Supergen, Inc., USA
 SO PCT Int. Appl., 38 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K031-00
 CC 1-6 (Pharmacology)
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001080843	A2	20011101	WO 2001-US12848	20010419
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6420378	B1	20020716	US 2000-553710	20000420 <--
PRAI	US 2000-553710	A1	20000420		
	US 1999-418862	A2	19991015	<--	
AB	A method for treating diseases assocd. with abnormal cell proliferation comprises delivering to a patient in need of treatment a compd. selected from 20(S)-camptothecin, an analog of 20(S)-camptothecin, a deriv. of 20(S)-camptothecin, a prodrug of 20(S)-camptothecin, and pharmaceutically active metabolite of 20(S)-camptothecin, in combination with an effective amt. of one or more agents selected from the group consisting of alkylating agent, antibiotic agent, antimetabolic agent, hormonal agent, plant-derived agent, anti-angiogenesis agent and biol. agent. The method can be used to treat benign tumors, malignant or metastatic tumors, leukemia and diseases assocd. with abnormal angiogenesis.				
ST	camptothecin cell proliferation inhibition tumor; metastasis tumor camptothecin cell proliferation inhibition; angiogenesis disease camptothecin cell proliferation inhibition; leukemia camptothecin cell proliferation inhibition; prodrug camptothecin cell proliferation inhibition				
IT	Macroglobulins RL: BSU (Biological study, unclassified); BIOL (Biological study) (2 macroglobulin-serum; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)				
IT	Angiogenic factors RL: BSU (Biological study, unclassified); BIOL (Biological study) (Ang-1, monoclonal antibodies to; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)				
IT	Angiogenic factors RL: BSU (Biological study, unclassified); BIOL (Biological study) (Ang-2, monoclonal antibodies to; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)				
IT	Gene, animal RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (BRCA2; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)				
IT	Gene, animal RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (BRCA; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)				
IT	Gene, animal RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				

- (DPC-4; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Papillomavirus
(E6 or E7 fragment; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E6, papillomavirus, fragment; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Transcription factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E7, papillomavirus, fragment; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(Ewing's sarcoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Hemocyanins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(KLH; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(Kaposi's sarcoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Gene, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NF-1; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Gene, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NF-2; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Disease, animal
(Oster Webber syndrome; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Gene, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RB1; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Gene, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

- study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TP53; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Gene, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(WT1; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(Wilms' tumor; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Kidney, neoplasm
(Wilms', inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Nerve, neoplasm
(acoustic neuroma, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(acoustic neuroma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(adenocarcinoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Liver, neoplasm
(adenoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Immunostimulants
(adjuvants; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Sulfonates
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkyl alkone; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Steroids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiostatic; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Nutrients
(anti-; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antiarteriosclerotics
(antiatherosclerotics; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Skin, neoplasm

- (basal cell carcinoma, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(basal cell carcinoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Biliary tract
(bile duct, neoplasm, adenoma and cystanoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(bone; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(brain; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(bronchi; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Adenoma
Adrenal gland, neoplasm
Alkylating agents, biological
Angiogenesis inhibitors
Anti-ischemic agents
Antibiotics
Antiglaucoma agents
Antirheumatic agents
Antiserums
Antitumor agents
Calculi, biliary
Carcinoid
Cell
Drug delivery systems
Hyperplasia
Immunomodulators
Mycobacterium BCG
Pheochromocytoma
Polycythemia vera
Psoriasis
(camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Carcinoembryonic antigen
Gangliosides
Interferons
Interleukin 12
Interleukin 2
Interleukin 4
Natural products
Prostate-specific antigen
.alpha.-Fetoproteins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(carcinoma, epidermoid; camptothecin or deriv., analog, metabolite, or

- prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(carcinoma, medullary carcinoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Neoplasm
(cell; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(cervix carcinoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Uterus, neoplasm
(cervix, carcinoma, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Uterus, disease
(cervix, dysplasia; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Intestine, neoplasm
(colon, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(colon; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Eye
(cornea, hyperplastic corneal nerve tumor; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Eye
(cornea, **transplant**; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT **Transplant and Transplantation**
(**cornea**; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT **Transplant rejection**
(corneal; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Brain
(cortex, cortical ischemia; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Eye, disease
(diabetic retinopathy; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Brain, disease
(edema, ischemic-reperfusion-related; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Uterus, disease
(endometriosis; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Lipopolysaccharides

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(endotoxin; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Toxins

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(endotoxins, lipopolysaccharides; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Neoplasm

(fibroma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Mycosis

(fungoides, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Antitumor agents

(gallbladder tumor inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Nerve, neoplasm

(ganglioneuroma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Antitumor agents

(giant cell tumor; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Neuroglia

(glioblastoma multiforme, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Antitumor agents

(glioblastoma multiforme; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Glycoproteins, specific or class

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(gp100; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Antitumor agents

(hairy cell leukemia; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Antitumor agents

(head; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Blood vessel, neoplasm

(hemangioma, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Antitumor agents

(hemangioma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations

- including camptothecin)
- IT Liver, neoplasm
(hepatoma, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(hepatoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Hormones, animal, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hormonal agents; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Neoplasm
(humoral hypercalcemia of malignancy; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Ovary, disease
(hyperplasia and hypervascularity; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunomodulating; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Bone, neoplasm
Brain, neoplasm
Kidney, neoplasm
Lung, neoplasm
Nerve, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Skin, neoplasm
Stomach, neoplasm
Thyroid gland, neoplasm
(inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Brain, disease
(injury, ischemic-reperfusion-related; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Ischemia
Reperfusion
(ischemic-reperfusion-related brain edema and injury; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(kidney; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(larynx tumor inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(leiomyoma inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

- IT Myoma
(leiomyoma, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Myoma
(leiomyoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(leukemia; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Adipose tissue, neoplasm
(lipoma, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(lipoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(lung small-cell carcinoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(lung; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(lymphocytic leukemia; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(lymphoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Eye, disease
(macula, degeneration; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(mammary gland; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(marfanoid habitus tumor; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antigens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(melanoma-assocd., MART-1; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(melanoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Mesothelium
(mesothelioma, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

- IT Antitumor agents
(mesothelioma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(metastasis, skin carcinoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Angiogenic factors
Hepatocyte growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(monoclonal antibodies to; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Skin, neoplasm
(mycosis fungoides, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(mycosis fungoides; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(myelogenous leukemia; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(myeloma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(myxoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(neck; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Bronchi
Head
Mammary gland
Neck, anatomical
Pancreatic islet of Langerhans
Prostate gland
(**neoplasm**, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Parathyroid gland
(neoplasm; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(nerve; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Nerve, neoplasm

- (neuroblastoma, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(neuroblastoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Schwann cell
(neurofibroma, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(neurofibroma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(neuroma inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Nerve, neoplasm
(neuroma, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Bone, neoplasm
(osteosarcoma, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
Bone, neoplasm
(osteosarcoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(ovary; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(pancreas; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(pancreatic islet; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Ovary, disease
(polycystic; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Proliferation inhibition
(proliferation inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(prostate gland; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Granuloma
(pyogenic; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Intestine, neoplasm
(rectum, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and

- combinations including camptothecin)
- IT Antitumor agents
(rectum; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Artery, disease
(restenosis; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Eye, neoplasm
(retinoblastoma, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(retinoblastoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Eye, disease
(retrolental fibroplasia; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(rhabdomyosarcoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(sarcoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Testis, neoplasm
(seminoma, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(seminoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(skin; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Lung, neoplasm
(small-cell carcinoma, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(soft tissue sarcoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Animal tissue
(soft, sarcoma, inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(squamous cell carcinoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Antitumor agents
(stomach; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT Peptidoglycans
Polysaccharides, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(sulfated polysaccharide peptidoglycan complex; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Protamines

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(sulfates; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Neoplasm

(teratoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Antitumor agents

(thyroid; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Eye, disease

(trachoma; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Gallbladder

Larynx

(tumor inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Gene, animal

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(tumor suppressor; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Antigens

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(tumor-assocd., monoclonal antibodies to; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Vaccines

(tumor; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Antitumor agents

(vaccines; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Interferons

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(.alpha.; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT Interferons

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(.beta.; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations

- including camptothecin)
- IT Interferons
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (.gamma.; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT 50-18-0, Cytosan 50-35-1, Thalidomide 50-44-2, Mercaptopurine 50-76-0, Dactinomycin 50-91-9, Floxuridine 51-21-8, Fluorouracil 52-67-5, D-Penicillamine 56-53-1, Diethylstilbestrol 57-22-7, Vincristine 58-05-9, Leucovorin 59-05-2, Methotrexate 76-43-7, Fluoxymesterone 125-84-8, Aminogluthethimide 127-07-1, Hydroxyurea 145-63-1, Suramin 147-94-4, Cytarabine 151-56-4D, Aziridine, derivs., biological studies 154-42-7, Thioguanine 302-79-4, Retinoic acid 334-22-5D, derivs. 362-07-2, 2-Methoxyestradiol 366-18-7, 2,2'-Bipyridine 444-27-9, Thiaprine 595-33-5, Megestrol acetate 618-27-9, cis-Hydroxyproline 865-21-4, Vinblastine 1119-28-4, .beta.-Aminopropionitrile fumarate 1398-61-4D, Chitin, sulfated derivs. 1404-00-8, Mitomycin 2133-34-8, L-Azetidine-2-carboxylic acid 3395-35-5, D,L-3,4-Dehydroproline 4291-63-8, Cladribine 7440-06-4D, Platinum, compds., biological studies 7689-03-4, 20(S)-Camptothecin 7689-03-4D, 20(S)-Camptothecin, analogs, derivs., metabolites, and prodrugs 9005-49-6, Heparin, biological studies 9015-68-3, Asparaginase 9076-44-2, Chymostatin 10540-29-1, Tamoxifen 11056-06-7, Bleomycin 11096-26-7, Erythropoietin 12244-57-4 13010-20-3D, Nitrosourea, derivs. 13311-84-7, Flutamide 14769-73-4, Levamisole 18378-89-7, Plicamycin 20830-81-3, Daunorubicin 23110-15-8, Fumagillin 23214-92-8, Doxorubicin 27988-97-2, Tetrazole 29767-20-2, Teniposide 33069-62-4, Paclitaxel 33419-42-0, Etoposide 34913-17-2 37270-94-3, Platelet factor 4 53643-48-4, Vindesine 53714-56-0, Leuprolide 53910-25-1, Pentostatin 56420-45-2, Epirubicin 58957-92-9, Idarubicin 62996-74-1, Staurosporine 63612-50-0, Nilutamide 64808-48-6, Lobenzarit disodium 65271-80-9, Mitoxantrone 65277-42-1, Ketoconazole 67699-40-5, Vinzolidine 71486-22-1, Vinorelbine 75607-67-9, Fludarabine phosphate 78186-34-2, Bisantrone 83150-76-9, Octreotide 83869-56-1, GM-CSF 84371-65-3, Mifepristone 84449-90-1, Raloxifene 86090-08-6, Angiostatin 89778-26-7, Toremifene 90357-06-5, Bicalutamide 91421-42-0, 9-Nitro-20(S)-camptothecin 91421-43-1, 9-Amino-20(S)-camptothecin 95058-81-4, Gemcitabine 108121-76-2, Anthracenedione 110124-55-5 114977-28-5, Docetaxel 121369-51-5, .beta.-Cyclodextrin tetradecasulfate 124861-55-8, TIMP-2 126509-46-4, Eponemycin 138757-15-0, .alpha.2-Antiplasmin 140208-23-7, PAI-1 140208-24-8, TIMP-1 142243-03-6, Proteinase inhibitor PAI-2 143011-72-7, G-CSF 145781-92-6, Goserelin acetate 148717-90-2, Squalamine 174722-31-7, Rituxan 180288-69-1, Herceptin 187888-07-9, Endostatin 371171-68-5, Chimp 3
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT 81669-70-7, Metalloproteinase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors; camptothecin or deriv., analog, metabolite, or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)
- IT 106096-92-8, Acidic fibroblast growth factor 106096-93-9
 , Basic fibroblast growth factor 129653-64-1, Fibroblast growth factor 5 188417-84-7, Vascular endothelial growth factor C
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (monoclonal antibodies to; camptothecin or deriv., analog, metabolite,

or prodrug thereof for inhibition of abnormal cell proliferation, and combinations including camptothecin)

IT 9001-12-1, Collagenase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.beta.-1-anticollagenase-serum; camptothecin or deriv., analog,
metabolite, or prodrug thereof for inhibition of abnormal cell
proliferation, and combinations including camptothecin)

L65 ANSWER 3 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 2001:416778 HCAPLUS

DN 135:24733

TI Pancreatic stem cells and their use in **transplantation**

IN Abraham, Elizabeth J.; Faustman, Denise; Habener, Joel L.; Vallejo, Mario;
Zulewski, Hendrik

PA General Hospital Corporation, USA

SO PCT Int. Appl., 102 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K035-00

ICS C12N015-85

CC 63-7 (Pharmaceuticals)

Section cross-reference(s): 1, 2, 15

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001039784	A1	20010607	WO 2000-US33031	20001206 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001024824	A1	20010927	US 2000-731255	20001206 <--
EP 1257282	A1	20021120	EP 2000-980985	20001206 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
PRAI US 1999-169082P	P	19991206	<--	
US 2000-215109P	P	20000628		
US 2000-238880P	P	20001006		
WO 2000-US33031	W	20001206		

AB Methods and compns. are described for the treatment of type I **insulin**-dependent diabetes mellitus and other conditions in a patient using newly identified stem cells that are capable of differentiation into a variety of pancreatic islet cells, including **insulin**-producing beta cells, as well as hepatocytes. Addnl., the patient may be treated with an immunosuppressant agent. Nestin has been identified as a mol. marker for pancreatic stem cells, while cytokeratin-19 serves as a marker for a distinct class of islet ductal cells. Methods are described whereby nestin-pos. stem cells can be isolated from pancreatic islets and cultured to obtain further stem cells or pseudo-islet like structures. Methods for ex vivo differentiation of the pancreatic stem cells are disclosed. Methods are described whereby pancreatic stem cells can be isolated, expanded, and **transplanted** into a patient in need thereof, either allogeneically, isogeneically or xenogeneically, to provide replacement for lost or damaged **insulin**-secreting cells or other cells. For example, a 3-fold stimulation of nestin mRNA levels in the islets cultured in high glucose compared to the islets cultured in normal glucose was obsd. Similarly, injection of glucagon-like peptide 1 (GLP-1) into mice was found to increase islet mass

by 2-fold in 48 h.

ST pancreas stem cell culture **transplant** diabetes immunosuppressant

IT Keratins
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (19; isolation, culture, and **transplantation** of pancreatic stem cells for diabetes treatment)

IT Transcription factors
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (IDX-1 (islet duodenum homeobox-1); isolation, culture, and **transplantation** of nestin-pos. pancreatic stem cells for diabetes treatment)

IT Nucleic acids
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (IDX-1-encoding; isolation, culture, and **transplantation** of nestin-pos. pancreatic stem cells for diabetes treatment)

IT Histocompatibility antigens
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (MHC (major histocompatibility complex), class I; differentiation of pancreatic stem cells that not express MHC antigens for diabetes treatment)

IT Histocompatibility antigens
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (MHC (major histocompatibility complex), class II; differentiation of pancreatic stem cells that not express MHC antigens for diabetes treatment)

IT **Transplant and Transplantation**
 (allotransplant, pancreas; isolation, culture, and **transplantation** of nestin-pos. pancreatic stem cells for diabetes treatment)

IT Pancreas
 (allotransplant; isolation, culture, and **transplantation** of nestin-pos. pancreatic stem cells for diabetes treatment)

IT **Transplant and Transplantation**
 (graft-vs.-host reaction; isolation, culture, and **transplantation** of nestin-pos. pancreatic stem cells for diabetes treatment)

IT Liver
 (hepatocyte; differentiation of pancreatic stem cells into hepatocyte)

IT Liver
 (identification of nestin-pos. pancreatic stem cells in liver)

IT Cell differentiation
 (inducers; isolation, culture, and **transplantation** of nestin-pos. pancreatic stem cells for diabetes treatment)

IT Drug delivery systems
 (injections, endoscopic retrograde; isolation, culture, and **transplantation** of nestin-pos. pancreatic stem cells for diabetes treatment)

IT Diabetes mellitus
 (insulin-dependent; isolation, culture, and **transplantation** of pancreatic stem cells for diabetes treatment)

IT Animal tissue culture
 Antidiabetic agents
 Cell differentiation
 Cell proliferation
 Immunosuppressants
 Rat
 Swine

- Transplant rejection**
(isolation, culture, and **transplantation** of nestin-pos. pancreatic stem cells for diabetes treatment)
- IT Hepatocyte growth factor
Lymphotoxin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(isolation, culture, and **transplantation** of nestin-pos. pancreatic stem cells for diabetes treatment)
- IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nestins; isolation, culture, and **transplantation** of nestin-pos. pancreatic stem cells for diabetes treatment)
- IT **Transplant and Transplantation**
(**pancreas**; isolation, culture, and **transplantation** of nestin-pos. pancreatic stem cells for diabetes treatment)
- IT Nerve
(stem cell; isolation, culture, and **transplantation** of nestin-pos. pancreatic stem cells but not neural stem cells for diabetes treatment)
- IT Pancreas
(stem cell; isolation, culture, and **transplantation** of nestin-pos. pancreatic stem cells for diabetes treatment)
- IT Antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(to GAD65; isolation, culture, and **transplantation** of nestin-pos. pancreatic stem cells and immunosuppressants for diabetes treatment)
- IT Pancreas
(**transplant**; isolation, culture, and **transplantation** of nestin-pos. pancreatic stem cells for diabetes treatment)
- IT Collagens, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type IV, antibodies against, labeled; isolation, culture, and **transplantation** of nestin-pos. pancreatic stem cells for diabetes treatment)
- IT Kidney
(xenogeneic **transplantation** of pancreatic stem cells into kidney)
- IT **Transplant and Transplantation**
(**xenotransplant, pancreas**; isolation, culture, and **transplantation** of nestin-pos. pancreatic stem cells for diabetes treatment)
- IT **Pancreatic islet of Langerhans**
(**.alpha.-cell**; isolation, culture, and **transplantation** of nestin-pos. pancreatic stem cells for diabetes treatment)
- IT **Pancreatic islet of Langerhans**
(**.beta.-cell**; isolation, culture, and **transplantation** of nestin-pos. pancreatic stem cells for diabetes treatment)
- IT 9024-58-2, Glutamate decarboxylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibodies to; isolation, culture, and **transplantation** of nestin-pos. pancreatic stem cells and immunosuppressants for diabetes treatment)
- IT 11028-71-0, Concanavalin A
RL: NUU (Other use, unclassified); USES (Uses)
(culture vessel coated with; isolation, culture, and **transplantation** of nestin-pos. pancreatic stem cells for diabetes treatment)
- IT 79217-60-0, Cyclosporin 104987-11-3, FK 506
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(isolation, culture, and **transplantation** of nestin-pos.
pancreatic stem cells and immunosuppressants for diabetes treatment)
IT 50-99-7, D-Glucose, biological studies 4449-51-8, Cyclopamine
62229-50-9, Epidermal growth factor 89750-14-1, Glucagon-like peptide I
104625-48-1, activin A **106096-93-9**, fibroblast growth factor 2
141732-76-5, exendin 4 148348-15-6, Fibroblast growth factor 7
163150-12-7, Betacellulin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(isolation, culture, and **transplantation** of nestin-pos.
pancreatic stem cells for diabetes treatment)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Beattie, G; J Clin Endocrin Met 1994, V78(5), P1232 HCAPLUS
- (2) Cornelius, J; Horm Met Res 1997, V29(6), P271 HCAPLUS
- (3) Hunziker, E; Biochem Biophys Res Comm 2000, V271(1), P116 HCAPLUS
- (4) Yasumizu, R; Proc Natl Acad Sci 1987, V84(18), P6555 MEDLINE

L65 ANSWER 4 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 2001:34737 HCAPLUS

DN 134:235321

TI Fibroblast growth factors are required for efficient tumor angiogenesis

AU Compagni, Amelia; Wilgenbus, Petra; Impagnatiello, Maria-Antonietta;
Cotten, Matt; Christofori, Gerhard

CS Research Institute of Molecular Pathology, Vienna, A-1030, Austria

SO Cancer Research (2000), 60(24), 7163-7169

CODEN: CNREA8; ISSN: 0008-5472

PB American Association for Cancer Research

DT Journal

LA English

CC 14-1 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 2

AB Although the function of vascular endothelial growth factor in the
induction of tumor angiogenesis is well understood, the role of a second
group of angiogenic factors, the fibroblast growth factors (FGFs), remains
elusive. We used a recombinant adenovirus expressing sol. FGF receptor
(AdsFGFR) to interfere with FGF function in tumor angiogenesis. AdsFGFR
repressed endothelial cell proliferation in vitro and inhibited tumor
angiogenesis in an ex vivo bioassay, in which endothelial cells were
cocultured with angiogenic tumor biopsies in a collagen gel. Moreover,
AdsFGFR repressed tumor angiogenesis and hence tumor growth in vivo in
allograft transplantation expts. Whereas adenoviral
expression of a sol. form of VEGF receptor 1 (AdsFlt) predominantly
affected the initiation of tumor angiogenesis, sol. FGF receptor (sFGFR)
appeared to impair the maintenance of tumor angiogenesis. The combination
of sFGFR and sol. Flt exhibited a synergistic effect in the repression of
tumor growth. Finally, i.v. injection of AdsFGFR resulted in a dramatic
repression of tumor growth in a transgenic mouse model of pancreatic
.beta. cell carcinogenesis. Similar to control infections with AdsFlt,
tumor-assocd. vessel d. was decreased, indicating that the expression of
sFGFR impaired tumor angiogenesis. These data indicate that FGFs play a
crit. role in tumor angiogenesis.

ST FGF receptor tumor angiogenesis

IT Angiogenesis

Cell proliferation

Transformation, neoplastic

(fibroblast growth factors are required for efficient tumor
angiogenesis)

IT Fibroblast growth factor receptors

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological
study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC
(Process)

(fibroblast growth factors are required for efficient tumor

- angiogenesis)
 IT Vascular endothelial growth factor receptors
 RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
 (gene flt 1; fibroblast growth factors are required for efficient tumor angiogenesis)
 IT **Pancreatic islet of Langerhans**
 (neoplasm; fibroblast growth factors are required for efficient tumor angiogenesis)
 IT Pancreas, neoplasm
 (.beta.-cell tumors; fibroblast growth factors are required for efficient tumor angiogenesis)
 IT **106096-92-8**
 RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
 (fibroblast growth factors are required for efficient tumor angiogenesis)
 IT 127464-60-2, Vascular endothelial growth factor
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (fibroblast growth factors are required for efficient tumor angiogenesis)

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
 RE

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L65 ANSWER 5 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:842288 HCAPLUS

DN 134:16530

TI Methods to inhibit infectious agent transmission during
xenotransplantation with fusion protein-encoding DNA

IN Federspiel, Mark J.

PA Mayo Medical Ventures, USA

SO PCT Int. Appl., 144 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C12N015-48

ICS C12N015-62; C07K014-15; C07K019-00; A61K048-00; C12Q001-68;
 C07K016-10; C12N007-01

CC 15-2 (Immunochemistry)

Section cross-reference(s): 3

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000071726	A1	20001130	WO 2000-US14296	20000524 <--
	WO 2000071726	C2	20020627		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRAI US 1999-135631P P 19990524 <--

AB The invention provides nucleic acid mols., compns. and methods to inhibit or prevent infectious agent transmission from donor to recipient or recipient to donor during or after **transplant**. The nucleic acids encode a fusion protein comprising a protein of the infectious agent and a degradative enzyme. For example, the infectious agent may be a virus such as pig endogenous retrovirus; the infectious agent protein may be a viral capsid protein, env glycoprotein, or accessory protein such as Vpr, Vif, and Nef; and the degradative enzyme may be a nuclease or protease. Thus, a gene encoding an avian leukosis virus (ALV) receptor protein fused to IgG was delivered and expressed by ALV-based retroviral vectors both in cultured cells and in chickens. The fusion protein significantly inhibited ALV infection in vitro and in vivo. The antiviral effect was specific for ALV, consistent with a receptor interference mechanism.

ST virus transmission **xenotransplantation** viral protein nuclease protease fusion

IT Proteins, specific or class

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses) (Vif, fusion proteins; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)

IT Proteins, specific or class

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses) (Vpx, fusion proteins; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)

- IT Antibodies
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(anti-pig endogenous retrovirus; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)
- IT Proteins, specific or class
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(capsid, fusion proteins; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)
- IT Kidney
Liver
Pancreas
(cell, **transplantation** of; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)
- IT Probes (nucleic acid)
RL: ARG (Analytical reagent use); PRP (Properties); ANST (Analytical study); USES (Uses)
(for detection of pig endogenous retrovirus; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)
- IT Envelope proteins
nef protein
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(fusion proteins; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)
- IT Proteins, specific or class
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(gene vpr, fusion proteins; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)
- IT Blood cell
(human, recombinant; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)
- IT Avian leukosis virus
Cytomegalovirus
Hepatitis virus
Herpesviridae
Human herpesvirus
Human herpesvirus 4
Human immunodeficiency virus
Lentivirus
Porcine endogenous retrovirus
Retroviridae
(infection by; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)
- IT Nerve
(neuron, **transplantation** of; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)
- IT cDNA sequences
(of pig endogenous retrovirus)
- IT Infection
(prevention of; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)
- IT Cell
(recombinant, fusion protein-producing; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)

- IT Organ, animal
(recombinant; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)
- IT Embryo, animal
(stem cell, **transplantation** of; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)
- IT Animal cell
(swine, recombinant; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)
- IT Heart
Kidney
Liver
Pancreatic islet of Langerhans
(**transplantation** of; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)
- IT **Transplant and Transplantation**
(**xenotransplant**; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)
- IT 257859-25-9
RL: ARG (Analytical reagent use); PRP (Properties); ANST (Analytical study); USES (Uses)
(amino acid sequence; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)
- IT **9001-62-1D**, Lipase, fusion protein 9001-92-7D, Proteinase, fusion protein 9001-99-4D, Ribonuclease, fusion protein 9026-12-4D, Barnase, fusion protein 9026-81-7D, Nuclease, fusion protein 9050-76-4D, Ribonuclease H, fusion protein
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)
- IT 247227-95-8 309306-82-9 309306-83-0 309306-84-1 309306-85-2
309306-86-3 309306-87-4
RL: ARG (Analytical reagent use); PRP (Properties); ANST (Analytical study); USES (Uses)
(nucleotide sequence; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)
- IT 216579-24-7 216579-31-6 216579-35-0 216579-40-7 309307-53-7, 1: PN: WO0071726 SEQID: 1 unclaimed DNA 309307-54-8, 2: PN: WO0071726 SEQID: 2 unclaimed DNA 309307-55-9, 6: PN: WO0071726 SEQID: 6 unclaimed DNA 309307-56-0, 7: PN: WO0071726 SEQID: 7 unclaimed DNA 309307-57-1 309307-58-2 309307-59-3 309307-60-6 309307-61-7 309307-62-8 309307-63-9 309307-64-0 309307-65-1 309307-66-2 309307-67-3 309307-68-4 309307-69-5 309307-70-8
RL: PRP (Properties)
(unclaimed nucleotide sequence; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)
- IT 198785-81-8 208129-24-2
RL: PRP (Properties)
(unclaimed protein sequence; methods to inhibit infectious agent transmission during **xenotransplantation** with fusion protein-encoding DNA)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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L65 ANSWER 6 OF 49 HCAPLUS COPYRIGHT 2002 ACS
 AN 2000:769087 HCAPLUS
 DN 133:329580
 TI Use of rosmarinic acid and derivatives thereof as immunosuppressants or inhibitors of SH2-mediated processes
 IN Hur, Eun Mi; Choi, Young Bong; Park, Changwon; Lee, Jongsung; Park, Dongsu; Yun, Yungdae; Lee, Keun Hyeung; Oh, Jong-Eun; Ahn, Soon Choul; Lee, Hyun Sun; Ahn, Jong Sok; Jung, Soo Il
 PA Mogam Biotechnology Research Institute, S. Korea
 SO U.S., 19 pp.
 CODEN: USXXAM
 DT Patent
 LA English
 IC ICM A61K031-235
 NCL 514533000
 CC 1-7 (Pharmacology)
 Section cross-reference(s): 25

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6140363	A	20001031	US 1999-312405	19990514 <--
	JP 2002526384	T2	20020820	JP 2000-549270	19990512 <--
PRAI	KR 1998-17741	A	19980516	<--	
	KR 1999-15989	A	19990504	<--	
	WO 1999-KR232	W	19990512	<--	
AB	The invention discloses the use of rosmarinic acid and/or derivs. thereof as immunosuppressive agents and/or inhibitors of SH2 domain function. Rosmarinic acid and derivs. thereof specifically inhibit the binding of ligand peptides to Lck SH2 domain, disturb the Lck-mediated signal transduction in T cells, also inhibit cytokine gene expression, and suppress immune responses in the transplanted tissue. These activities of rosmarinic acid and derivs. thereof support their applicability to treatment, prevention and/or diagnosis of graft rejection, graft -vs.-host disease, autoimmune diseases, inflammatory diseases, etc.				
ST	rosmarinic acid deriv prepn immunosuppressant; Lck SH2 domain inhibition rosmarinic acid				
IT	Antibodies RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (OKT-3; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)				
IT	Protein motifs (SH2 domain; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)				
IT	Cytotoxic agents (T-cell; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)				
IT	Antiserums (anti-lymphocyte/thymocyte; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)				
IT	Interleukin 2 receptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (antibodies to; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)				
IT	Lymphocyte (antisera to; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)				
IT	Immunoglobulins				

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antithymocyte globulins; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT **Transplant and Transplantation**

Transplant and Transplantation

(bone marrow; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT Muscle, disease

(breakdown; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT Musculoskeletal diseases

Musculoskeletal diseases

(cartilage, increased absorption; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT Eye

Eye

(cornea, **transplant**; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT **Transplant and Transplantation**

(cornea; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT Gene, animal

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(cytokine; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT Cartilage

Cartilage

(disease, increased absorption; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT Joint, anatomical

(disease, joint destruction; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT Adipose tissue

(elevated fat level; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT Gene

(expression, cytokine; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT Cytokines

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(genes, expression; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT **Transplant and Transplantation**

(graft-vs.-host reaction;

rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT **Transplant and Transplantation**

(heart valve; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT **Transplant and Transplantation**

Transplant and Transplantation

(heart; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT **Transplant and Transplantation**

Transplant and Transplantation

(kidney; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT Antitumor agents

(leukemia; rosmarinic acid and derivs. as immunosuppressants and

- inhibitors of SH2-mediated processes)
- IT **Transplant and Transplantation**
Transplant and Transplantation
(liver; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)
- IT **Transplant and Transplantation**
Transplant and Transplantation
(lung; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)
- IT **Transplant and Transplantation**
Transplant and Transplantation
(pancreas; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)
- IT **Transplant and Transplantation**
Transplant and Transplantation
(pancreatic islet; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)
- IT Proliferation inhibition
(proliferation inhibitors, T-cell; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)
- IT Anti-AIDS agents
Anti-Alzheimer's agents
Anti-infective agents
Antiartherosclerotics
Anticoagulants
Antidiabetic agents
Antirheumatic agents
Autoimmune disease
Diagnosis
Hepatitis
Human immunodeficiency virus
Immunosuppressants
Lupus erythematosus
Meningitis
Myasthenia gravis
Prunella vulgaris
Psoriasis
Signal transduction, biological
T cell (lymphocyte)
Transplant rejection
(rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)
- IT Corticosteroids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)
- IT Interleukin 1.beta.
Interleukin 2
Interleukin 4
Interleukin 6
TCR (T cell receptors)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)
- IT **Transplant and Transplantation**
Transplant and Transplantation
(skin; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)
- IT **Transplant and Transplantation**
(small intestine; rosmarinic acid and derivs. as

immunosuppressants and inhibitors of SH2-mediated processes)

IT Intestine
Intestine
(small, **transplant**; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT Drug interactions
(synergistic; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT Multiple sclerosis
(therapeutic agents; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT Thymus gland
(thymocyte, antisera to; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT Bone marrow
Bone marrow
Heart
Heart
Kidney
Kidney
Liver
Liver
Lung
Lung
Pancreas
Pancreas
Pancreatic islet of Langerhans
Pancreatic islet of Langerhans
Skin
Skin
(**transplant**; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT Heart
Heart
(valve, **transplant**; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT Interferons
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.gamma.; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT 114051-78-4, Lck kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(SH2 domain; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT 179188-11-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(osmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT 32483-30-0P 42085-50-7P 136749-43-4P 203118-25-6P 203118-32-5P
303175-71-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT 60-18-4, (S)-Tyrosine, reactions 64-17-5, Ethanol, reactions 67-63-0, Isopropyl alcohol, reactions 75-36-5, Acetyl chloride 106-95-6, Allyl bromide, reactions 331-39-5, Caffeic acid 69739-34-0, tert-Butyldimethylsilyl triflate
RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction; rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT 154447-36-6, LY294002
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT 179462-74-9P, .+-.Rosmarinic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT 118120-95-9P 303175-68-0P 303175-69-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT 50-18-0, Cyclophosphamide 59-05-2, Methotrexate 446-86-6, Azathioprine 24280-93-1, Mycophenolic acid 50924-49-7, Mizoribine 53123-88-9, Rapamycin 59122-46-2, Misoprostol 59865-13-3, Cyclosporin A 59865-13-3D, Cyclosporin A, derivs. 75706-12-6, Leflunomide 89149-10-0, 15-Deoxyspergualin 104987-11-3, FK-506 104987-11-3D, FK-506, derivs. 128794-94-5 179462-74-9D, .+-.Rosmarinic acid, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT 7440-70-2, Calcium, biological studies 303175-72-6
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(rosmarinic acid and derivs. as immunosuppressants and inhibitors of SH2-mediated processes)

IT 304488-47-9, 1: PN: US6140363 SEQID: 1 unclaimed DNA 304488-48-0, 2: PN: US6140363 SEQID: 2 unclaimed DNA 304488-49-1, 3: PN: US6140363 SEQID: 3 unclaimed DNA 304488-50-4, 4: PN: US6140363 SEQID: 4 unclaimed DNA 304488-51-5, 5: PN: US6140363 SEQID: 5 unclaimed DNA 304488-52-6, 6: PN: US6140363 SEQID: 6 unclaimed DNA 304488-53-7, 7: PN: US6140363 SEQID: 7 unclaimed DNA 304488-54-8, 8: PN: US6140363 SEQID: 8 unclaimed DNA 304488-55-9, 9: PN: US6140363 SEQID: 9 unclaimed DNA 304488-56-0 304488-57-1 304488-58-2
RL: PRP (Properties)
(unclaimed nucleotide sequence; use of rosmarinic acid and derivs. thereof as immunosuppressants or inhibitors of SH2-mediated processes)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Christ; US 4354035 1982 HCAPLUS
(2) Wirtz-Peitz; US 4358442 1982 HCAPLUS
(3) Zenk; US 4329361 1982 HCAPLUS

L65 ANSWER 7 OF 49 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:725482 HCAPLUS
DN 133:276356
TI Use of ErbB receptor ligands in treating diabetes
IN Huang, Xiaojian; Stewart, Timothy Andrew
.PA Genentech, Inc., USA
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent

LA English
 IC ICM A61K038-00
 CC 1-10 (Pharmacology)
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000059525	A2	20001012	WO 2000-US9240	20000405 <--
	WO 2000059525	A3	20010208		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP	1165113	A2	20020102	EP 2000-921827	20000405 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
	JP 2002541117	T2	20021203	JP 2000-609088	20000405 <--
PRAI	US 1999-128017P	P	19990406 <--		
	WO 2000-US9240	W	20000405		
AB	The invention provides methods for treating pancreatic dysfunction, particularly diabetes, in mammals using ErbB receptor ligands, such as heregulin, betacellulin, and EGF. Methods of treating such conditions using anti-ErbB receptor agonist antibodies are further provided. The methods of the invention may be performed by direct administration of such therapeutically useful agents to mammals, or alternatively, by exposing certain pancreatic cell types to such agents in vitro and subsequently transplanting the treated cells to a mammal.				
ST	ErbB receptor ligand treatment diabetes; pancreas disfunction treatment heregulin betacellulin EGF; antibody ErbB receptor agonist antidiabetic; transplantation pancreas ErbB receptor ligand				
IT	Transplant and Transplantation Transplant and Transplantation (allotransplant, pancreas; use of ErbB receptor ligands in treating diabetes)				
IT	Pancreas (allotransplant; use of ErbB receptor ligands in treating diabetes)				
IT	Medical goods (cannulas; use of ErbB receptor ligands in treating diabetes)				
IT	Pancreas, disease (dysfunction; use of ErbB receptor ligands in treating diabetes)				
IT	Ligands RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (for ErbB receptor; use of ErbB receptor ligands in treating diabetes)				
IT	Gene, animal RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence) (for heregulin or ErbB2 or ErbB3, mice heterozygous for; use of ErbB receptor ligands in treating diabetes)				
IT	Diabetes mellitus (insulin-dependent; use of ErbB receptor ligands in treating diabetes)				
IT	Epidermal growth factor receptors RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ligands; use of ErbB receptor ligands in treating diabetes)				

IT **Transplant and Transplantation**
Transplant and Transplantation
 (pancreatic islet; use of ErbB receptor ligands in treating diabetes)

IT Antibodies
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (to ErbB receptor agonists; use of ErbB receptor ligands in treating diabetes)

IT **Pancreatic islet of Langerhans**
Pancreatic islet of Langerhans
 (transplant; use of ErbB receptor ligands in treating diabetes)

IT Diabetes mellitus
 Drug delivery systems
 Immunosuppressants
 Immunotherapy
 Mammal (Mammalia)
 (use of ErbB receptor ligands in treating diabetes)

IT Heregulins
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (use of ErbB receptor ligands in treating diabetes)

IT Transforming growth factors
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (.alpha.-; use of ErbB receptor ligands in treating diabetes)

IT **Pancreatic islet of Langerhans**
 (.beta.-cell; use of ErbB receptor ligands in treating diabetes)

IT 62229-50-9, EGF 117147-70-3, Amphiregulin 154531-34-7
 163150-12-7, Betacellulin
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (use of ErbB receptor ligands in treating diabetes)

L65 ANSWER 8 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:573837 HCAPLUS

DN 133:191991

TI Humanized immunoglobulin reactive with B7 molecules and methods of treatment therewith

IN Co, Man Sung; Vasquez, Maximiliano; Carreno, Beatriz; Celniker, Abbie Cheryl; Collins, Mary; Goldman, Samuel; Gray, Gary S.; Knight, Andrea; O'Hara, Denise; Rup, Bonita; Veldman, Geertruida M.

PA Genetics Institute, Inc., USA

SO PCT Int. Appl., 162 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07K016-28

ICS C12N005-10; C12N015-62; C12N015-13; G01N033-68; G01N033-577;
 A61K039-395; A61K035-12; A61P035-00; A61P007-06; A61P003-00;
 A61P037-00; A61P025-00; A61P001-18; A61P019-02; A61P001-00;
 A61P017-00; A61K039-505; A61K038-13; A61K031-445

CC 15-3 (Immunochemistry)

Section cross-reference(s): 3

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000047625	A2	20000817	WO 2000-US3303	20000209 <--

WO 2000047625 A3 20010802
 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002176855 A1 20021128 US 1999-249011 19990212 <--

EP 1159300 A2 20011205 EP 2000-919275 20000209 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

BR 2000008209 A 20020219 BR 2000-8209 20000209 <--

NO 2001003911 A 20011010 NO 2001-3911 20010810 <--

PRAI US 1999-249011 A 19990212 <--

US 1999-339596 A2 19990624 <--

WO 2000-US3303 W 20000209

AB The invention relates to humanized anti-B7-2 and anti-B7-1 antibodies, wherein each comprise a variable region of non-human origin and at least a portion of an Ig of human origin. The invention also pertains to methods of treatment for various autoimmune diseases, **transplant** rejection, inflammatory disorders and infectious diseases by administering humanized anti-B7-2 and/or anti-B7-1 antibodies.

ST humanized Ig antigen B7 autoimmune disease

IT Animal cell line
 (ATCC CRL-12524 and PTA-263; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT **Receptors**

RL: BSU (Biological study, unclassified); BIOL (Biological study) (B7-1; humanized **Ig**. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT Glycoproteins, specific or class

RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD40-L (antigen CD40 ligand); humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT Immunoglobulins

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (G, human const. or framework; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT Immunoglobulins

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (G2, human const. or framework; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT Immunoglobulins

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (G4, human const. or framework; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT Histocompatibility antigens

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (MHC (major histocompatibility complex), class I; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases,

- inflammation, **transplant** rejection, and infections)
- IT Chimeric gene
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (animal; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)
- IT Interleukin 2 receptors
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antagonists; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)
- IT Anemia (disease)
 (aplastic; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)
- IT **Transplant and Transplantation**
Transplant and Transplantation
 (bone marrow; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)
- IT Gene, animal
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (chimeric; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)
- IT Blood products
 (component **transplant**; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)
- IT Gene therapy
 (delivery vector; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)
- IT Metabolism, animal
 (disorder, inborn; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)
- IT Immunoglobulins
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (heavy chains, humanized; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)
- IT Immunodeficiency
 (hereditary; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)
- IT Adeno-associated virus
 Anemia (disease)
 Arthritis
 Asthma
 Autoimmune disease
 DNA sequences
 Diabetes mellitus
 Drug delivery systems
 Drugs
 Genetic vectors
 Hematopoiesis
 Immunomodulators

Immunosuppressants
 Immunotherapy
 Infection
 Inflammation
 Leukemia
 Lymphocyte
 Lymphoma
 Mammal (Mammalia)
 Molecular cloning
 Mouse
 Multiple sclerosis
 Neoplasm
 Protein sequences
 Retroviridae
 Rodent
 Sick cell anemia
 Thalassemia

Transplant rejection

(humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT Nucleic acids

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT Antigens

CD80 (antigen)

CD86 (antigen)

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT CD40 (antigen)

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT Steroids, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT Antibodies

Immunoglobulins

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(humanized; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT Immune tolerance

(induction; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT Dermatitis

Intestine, disease

(inflammatory; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT **Pancreatic islet of Langerhans**

(**insulinitis**; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT Immunoglobulins

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(light chains, humanized; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT **Antibodies**

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(**monoclonal**, 3D1 and 1F1; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT **Myeloproliferative disorders**

(myelodysplasia; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT **Blood**

(peripheral; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT **Disease, animal**

(proliferative; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT **Cell**

(stem; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT **Lupus erythematosus**

(systemic; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT **Toxoids**

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(tetanus; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT **Blood cell**

Bone marrow

Bone marrow

(**transplant**; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT **DNA**

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(vector; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT 288406-94-0P 288406-95-1P 288406-96-2P 288406-97-3P 288406-98-4P
288406-99-5P 288407-00-1P 288407-01-2P

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(amino acid sequence; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT 53-03-2, Prednisone 59-05-2, Methotrexate 1247-42-3, Methyl prednisone
9001-28-9, Blood coagulation factor IX 9002-72-6, Growth hormone
9004-10-8, **Insulin**, biological studies 53123-88-9,
Rapamycin 59865-13-3, Cyclosporine 63798-73-2, Cyclosporine
104987-11-3, FK 506 113189-02-9 128794-94-5, Mycophenolate mofetil

152923-56-3 179045-86-4, Simulect
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT 9025-75-6, Calcineurin
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (inhibitor; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT 288637-71-8P 288637-72-9P 288637-73-0P 288637-74-1P 288637-75-2P
 288637-76-3P 288637-77-4P 288637-78-5P
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (nucleotide sequence; humanized Ig. reactive with B7 mols. for treatment of autoimmune diseases, inflammation, **transplant** rejection, and infections)

IT 141977-02-8 246223-23-4 288390-77-2 288390-78-3 288390-79-4
 288390-80-7 288390-82-9 288390-83-0 288390-84-1 288390-85-2
 288390-86-3 288390-87-4
 RL: PRP (Properties)
 (unclaimed sequence; humanized Ig reactive with B7 mols. and methods of treatment therewith)

L65 ANSWER 9 OF 49 HCAPLUS COPYRIGHT 2002 ACS
 AN 2000:554496 HCAPLUS
 DN 134:236138
 TI Porcine **islets** of **Langerhans** isolated from normal and hDAF transgenic pigs elicit the same acute inflammatory reaction during exposure to human blood; inhibition of the response with soluble complement receptor 1 and **heparin**

AU **Bennet, W.**; Sundberg, B.; Song, Z.; Elgue, G.; Wennberg, L.; Richards, A.; White, D. J.; **Larsson, R.**; **Nilsson, B.**; Groth, C.-G.; **Korsgren, O.**

CS Karolinska Institute, Department of Transplantation Surgery, Huddinge Hospital, Huddinge, Swed.

SO Transplantation Proceedings (2000), 32(5), 1065
 CODEN: TRPPA8; ISSN: 0041-1345

PB Elsevier Science Inc.
 DT Journal
 LA English
 CC 15-10 (Immunochemistry)

AB Porcine **islets** exposed to fresh human blood in vitro has been previously obsd. to elicit an immediate inflammatory reaction, resulting in disruption of **islet** integrity. Complement inhibition prevents hyperacute rejection of vascularized discordant **xenografts**. A study was conducted to investigate whether inhibition of the complement and coagulation systems in human blood affected the outcome of porcine **islet** damage. It was also tested whether **islets** from a single founder line of hDAF transgenic (TG) pigs are protected from this reaction. **Islets** of **Langerhans** from adult and fetal pigs exposed to human blood triggered an injurious, inflammatory response. A similar response was elicited by **islets** from hDAF TG pigs. The inflammatory response could be significantly reduced by adding inhibitors of the complement and coagulation systems.

ST islet **xenotransplantation** pig human complement receptor **heparin** inflammation

IT Coagulation
 Inflammation
 Pancreatic islet of Langerhans

(acute inflammatory reaction in **xenotransplantation** of porcine **islets** and its inhibition with sol. complement receptor 1 and **heparin**)

IT Embryo, animal
(fetus; acute inflammatory reaction in **xenotransplantation** of porcine islets and its inhibition with sol. complement receptor 1 and **heparin**)

IT Complement receptors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(type 1; acute inflammatory reaction in **xenotransplantation** of porcine islets and its inhibition with sol. complement receptor 1 and **heparin**)

IT **Transplant and Transplantation**
(**xenotransplant**; acute inflammatory reaction in **xenotransplantation** of porcine islets and its inhibition with sol. complement receptor 1 and **heparin**)

IT **9005-49-6, Heparin, biological studies**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(acute inflammatory reaction in **xenotransplantation** of porcine islets and its inhibition with sol. complement receptor 1 and **heparin**)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Bennet, W; to be published in Transplantation
- (2) Carrington, C; Transplant Proc 1995, V27, P321 HCAPLUS
- (3) Pruitt, S; Transplantation 1997, V63, P900 HCAPLUS
- (4) White, D; XENO 1995, V3, P48

L65 ANSWER 10 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:553433 HCAPLUS

DN 133:168453

TI Use of a clot preventing agent with **transplanted** cell and tissues

IN **Korsgren, Olle; Bennet, William; Nilsson, Bo**
; Larsson, Rolf

PA **Corline Systems AB, Swed.**

SO PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K038-36

ICS A61K038-55; C12N005-06; C07K014-745

CC 63-8 (Pharmaceuticals)

Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000045837	A1	20000810	WO 2000-SE223	20000204 <--
	W:				
	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,				
	CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE,				
	GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,				
	LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,				
	RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,				
	US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE,				
	DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,				
	CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	SE 9900398	A	20000806	SE 1999-398	19990205 <--
	EP 1171156	A1	20020116	EP 2000-906843	20000204 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO

PRAI SE 1999-398 A 19990205 <--
WO 2000-SE223 W 20000204 <--

AB The present invention is within the field of **transplantation** surgery. More closely, the present invention relates to use of a clotting preventing agent in the prodn. of a drug for administration in assocn. with **transplantation of insulin** producing cells in the form of isolated **islets** to patients with **insulin** dependent diabetes mellitus, IDDM. The invention is expected to significantly improve the clin. outcome of **transplantation of islets of Langerhans**. **Langerhans islets** induced aggradation of platelets when they were added to platelet rich plasma. Addn. of **RGDS** peptide to plasma totally abolished the aggregation and the consumption of platelets.

ST clot prevention **transplant** cell tissue; **langerhans islet transplant** peptide platelet aggregation

IT Platelet (blood)
(aggregation; use of clot preventing agent with **transplanted** cell and tissues)

IT Diabetes mellitus
(**insulin**-dependent; use of clot preventing agent with **transplanted** cell and tissues)

IT **Antibodies**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**monoclonal**; use of clot preventing agent with **transplanted** cell and tissues)

IT **Anticoagulants**
Pancreatic islet of Langerhans
Platelet aggregation inhibitors
Surgery
Transplant and Transplantation
(use of clot preventing agent with **transplanted** cell and tissues)

IT **Immunoglobulin receptors**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of clot preventing agent with **transplanted** cell and tissues)

IT **9005-49-6, Heparin**, biological studies 91037-65-9
99896-85-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of clot preventing agent with **transplanted** cell and tissues)

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L65 ANSWER 11 OF 49 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:426869 HCAPLUS
DN 133:64074

TI Medical implants containing angiogenic factors which provide space for cell **transplant**, sensor implantation, etc.

IN Iwata, Hiroo; Inoue, Kazutomo; Ikada, Yoshito

PA Kyoto University, Japan

SO Jpn. Kokai Tokkyo Koho, 8 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

IC ICM A61K009-00

ICS A61K038-00

CC 63-7 (Pharmaceuticals)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2000178180	A2	20000627	JP 1998-354287	19981214 <--
	JP 3089299	B2	20000918		
AB	The implant, which provides a space around which capillary bed (tissues rich in capillary vessels) are formed, comprises a base made from hydrogel, etc., and angiogenic factors. A polyethylene film inserted into a polyester mesh bag was impregnated with a soln. contg. poly(vinyl alc.), glutaraldehyde, and HCl to form poly(vinyl alc.) gel. A phosphate-buffered saline contg. agarose, hyaluronic acid, and basic FGF was injected into the above gel. The bag was s.c. implanted to a streptozotocin-induced diabetic rat and removed after 1 wk to form a space, into which isolated Langerhans islets were transplanted to normalize blood sugar.				
ST	capillary bed induction removable implant hydrogel angiogenic factor; bFGF polyvinyl alc gel cell transplant space providing implant				
IT	Medical goods (bags; medical implants contg. angiogenic factors to provide space around which capillary bed is formed, for cell transplant and sensor implantation)				
IT	Polyester fibers, biological studies RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (fabrics, mesh, bag; medical implants contg. angiogenic factors to provide space around which capillary bed is formed, for cell transplant and sensor implantation)				
IT	Capillary vessel Hydrogels Sensors Transplant and Transplantation (medical implants contg. angiogenic factors to provide space around which capillary bed is formed, for cell transplant and sensor implantation)				
IT	Angiogenic factors Osteonectin Platelet-derived growth factors RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (medical implants contg. angiogenic factors to provide space around which capillary bed is formed, for cell transplant and sensor implantation)				
IT	Angiogenesis (neovascularization; medical implants contg. angiogenic factors to provide space around which capillary bed is formed, for cell transplant and sensor implantation)				
IT	Transforming growth factors RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (.beta.-; medical implants contg. angiogenic factors to provide space around which capillary bed is formed, for cell transplant and				

- sensor implantation)
 IT 9002-89-5 9012-36-6, Agarose
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (gel; medical implants contg. angiogenic factors to provide space
 around which capillary bed is formed, for cell **transplant** and
 sensor implantation)
- IT 106096-92-8 106096-93-9 127464-60-2, Vascular
 endothelial growth factor 186270-49-5, Angiopoietin 1 194368-66-6,
 Angiopoietin 2
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
 (Uses)
 (medical implants contg. angiogenic factors to provide space around
 which capillary bed is formed, for cell **transplant** and sensor
 implantation)
- L65 ANSWER 12 OF 49 HCAPLUS COPYRIGHT 2002 ACS
 AN 2000:356109 HCAPLUS
 DN 134:16089
 TI Effects of diabetes and hypoxia on gene markers of angiogenesis (HGF,
 cMET, uPA and uPAR, TGF-.alpha., TGF-.beta., bFGF and Vimentin) in
 cultured and **transplanted** rat islets
 AU Vasir, B.; Reitz, P.; Xu, G.; Sharma, A.; Bonner-Weir, S.; Weir, G. C.
 CS Joslin Diabetes Center and Department of Medicine, Research Division,
 Section on Islet Transplantation and Cell Biology, Harvard Medical School,
 Boston, MA, USA
 SO Diabetologia (2000), 43(6), 763-772
 CODEN: DBTGAI; ISSN: 0012-186X
 PB Springer-Verlag
 DT Journal
 LA English
 CC 14-8 (Mammalian Pathological Biochemistry)
 AB The vascularization of newly **transplanted** islets originates from
 the recipients. Because islets **transplanted** into a diabetic do
 less well than those **transplanted** into a euglycemic environment,
 the authors examd. the hypothesis that gene expression of angiogenic
 factors in **grafts** is delayed in diabetes. These factors include
 hepatocyte growth factor (HGF) and its receptor c-MET, and urokinase
 plasminogen activator (uPA) and its receptor uPAR, basic fibroblast growth
 factor (bFGF), TGF-.alpha. and TGF.beta.-1. Isolated rat islets were
 studied in vitro under normoxic and hypoxic culture conditions and gene
 expression was detd. with semi-quant. multiplex RT-PCR. The authors found
 that HGF but not c-MET expression was induced by hypoxia in vitro. Using
 syngeneic Lewis rats, gene expression was also studied in **grafts**
 on days 1, 3, 5, 7 and 14 after **transplantation**. In
grafts of normoglycemic rats, HGF expression was enhanced on day 3
 and maintained whereas expression of c-MET fell and remained down until
 day 14. Expression of uPA was up at day 3 and remained high; expression
 of uPAR was also up at day 3 but then fell to control levels at day 14.
 Expression of bFGF, TGF-.alpha. and TGF.beta.-1 persisted throughout.
 Vimentin, a marker of fibroblasts, had increased expression at day 1 which
 was further enhanced in subsequent days. In the **grafts** of
 diabetic recipients the expression of HGF, uPA and uPAR were delayed,
 being clearly expressed at day 5 rather than day 3. Vimentin expression
 was similarly delayed. This apparent delay in angiogenesis provides a
 potential mechanism for the less favorable outcomes of islets
transplanted into diabetic recipients.
- ST diabetes islet **transplant** angiogenesis fibroblast vimentin; uPA
 uPAR islet **transplant** angiogenesis diabetes; TGF islet
transplant angiogenesis diabetes; HGF cMET islet
transplant angiogenesis diabetes; bFGF islet **transplant**
 angiogenesis diabetes
- IT Hepatocyte growth factor receptors

- RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cMET; diabetes and hypoxia effect on angiogenesis marker expression in cultured and **transplanted** islets)
- IT Vimentins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(diabetes and hypoxia effect on angiogenesis marker expression and fibroblasts in cultured and **transplanted** islets)
- IT Hepatocyte growth factor
Urokinase-type plasminogen activator receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(diabetes and hypoxia effect on angiogenesis marker expression in cultured and **transplanted** islets)
- IT Angiogenesis
Hypoxia, animal
(diabetes and hypoxia effect on angiogenesis marker expression of in cultured and **transplanted** islets)
- IT **Transplant and Transplantation**
(**pancreatic islet**; diabetes and hypoxia effect on angiogenesis marker expression in cultured and **transplanted** islets)
- IT **Pancreatic islet of Langerhans**
(**transplant**; diabetes and hypoxia effect on angiogenesis marker expression in cultured and **transplanted islets**)
- IT Transforming growth factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.alpha.-; diabetes and hypoxia effect on angiogenesis marker expression in cultured and **transplanted** islets)
- IT Transforming growth factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.beta.-; diabetes and hypoxia effect on angiogenesis marker expression in cultured and **transplanted** islets)
- IT **106096-93-9**, Basic fibroblast growth factor
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(diabetes and hypoxia effect on angiogenesis marker expression and fibroblasts in cultured and **transplanted** islets)
- IT **139639-24-0**, Urokinase type plasminogen activator
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(diabetes and hypoxia effect on angiogenesis marker expression in cultured and **transplanted** islets)

RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD
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- L65 ANSWER 13 OF 49 HCAPLUS COPYRIGHT 2002 ACS
 AN 2000:280885 HCAPLUS
 DN 133:280536
 TI Pancreatic islet **xenograft** tolerance after short-term
 costimulation blockade is associated with increased CD4+ T cell apoptosis
 but not immune deviation
 AU Lehnert, Anne M.; Yi, Shounan; Burgess, Jane S.; O'Connell, Philip J.
 CS National Pancreas Transplant Unit, University of Sydney at Westmead
 Hospital, Westmead, 2145, Australia
 SO Transplantation (2000), 69(6), 1176-1185
 CODEN: TRPLAU; ISSN: 0041-1337
 PB Lippincott Williams & Wilkins
 DT Journal
 LA English
 CC 15-10 (Immunochemistry)
 AB The authors' purpose was to det. if short-term inhibition of the
 CD40/CD40L and CD28/B7 costimulatory pathways was capable of inducing
 specific unresponsiveness to pancreatic islet **xenografts** and to
 ascertain the mechanism of tolerance induction. Diabetic B6AF1 mice were
transplanted with Wistar or DA rat islets and were treated short
 term with CTLA4-Fc and anti-CD40L **mAb** (MR1).
 Coadministration of CTLA4-Fc with MR1 resulted in indefinite rat
 islet **xenograft** survival in mice. Tolerance was species but not
 strain specific as long-term surviving recipients rejected third party

BALB/c islet **allografts** but accepted a second rat islet **xenograft** from the same or different donor strain. Tolerance induction was assocd. with a large leukocyte infiltrate that did not exhibit features of immune deviation as **intragraft** T cell-specific cytokine gene expression was globally reduced. In particular, interleukin-4 gene expression was markedly suppressed. There was a complete inhibition of anti-donor IgG, IgG1, and IgM antibody in the serum of CTLA4-**Fc**/MR1-treated animals. Tolerance induction was assocd. with increased CD4+ T cell apoptosis as there was an increased proportion of annexin-V staining and Fas expressing CD4+ T cells and a decrease in CD4+ T cell Bcl-2 expression in the **grafts** and draining lymph nodes of CTLA4-**Fc**/MR1-treated recipients. Combined costimulatory blockade was capable of producing tolerance to pancreatic islet **xenografts**. The induction of this tolerant state was assocd. with increased T cell apoptosis, whereas the maintenance phase of tolerance was assocd. with the accumulation of a large no. of inactive lymphocytes within the **graft**.

- ST pancreas **xenograft** tolerance costimulatory mol blockade
 IT Glycoproteins, specific or class
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (CD40-L (antigen CD40 ligand); pancreatic islet **xenograft**
 tolerance after short-term costimulation blockade is assocd. with
 increased CD4+ T cell apoptosis but not immune deviation)
- IT **Immunoglobulins**
 RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL
 (Biological study); FORM (Formation, nonpreparative)
 (G1; pancreatic islet **xenograft** tolerance after short-term
 costimulation blockade is assocd. with increased CD4+ T cell apoptosis
 in relation to)
- IT **Immunoglobulins**
 RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL
 (Biological study); FORM (Formation, nonpreparative)
 (G; pancreatic islet **xenograft** tolerance after short-term
 costimulation blockade is assocd. with increased CD4+ T cell apoptosis
 in relation to)
- IT **Immunoglobulins**
 RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL
 (Biological study); FORM (Formation, nonpreparative)
 (M; pancreatic islet **xenograft** tolerance after short-term
 costimulation blockade is assocd. with increased CD4+ T cell apoptosis
 in relation to)
- IT Leukocyte
 (infiltration; pancreatic islet **xenograft** tolerance after
 short-term costimulation blockade is assocd. with increased CD4+ T cell
 apoptosis in relation to)
- IT Cell migration
 (leukocyte infiltration; pancreatic islet **xenograft** tolerance
 after short-term costimulation blockade is assocd. with increased CD4+
 T cell apoptosis in relation to)
- IT Apoptosis
 CD4-positive T cell
 Immune tolerance
 (pancreatic islet **xenograft** tolerance after short-term
 costimulation blockade is assocd. with increased CD4+ T cell apoptosis
 but not immune deviation)
- IT CD28 (antigen)
 CD40 (antigen)
 CD80 (antigen)
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (pancreatic islet **xenograft** tolerance after short-term
 costimulation blockade is assocd. with increased CD4+ T cell apoptosis
 but not immune deviation)
- IT Interleukin 4

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (pancreatic islet **xenograft** tolerance after short-term
 costimulation blockade is assocd. with increased CD4+ T cell apoptosis
 in relation to)

IT **Transplant and Transplantation**
Transplant and Transplantation

(**xenotransplant**, islet of
Langerhans; **pancreatic islet**
xenograft tolerance after short-term costimulation blockade is
 assocd. with increased CD4+ T cell apoptosis but not immune deviation)

IT **Pancreatic islet of Langerhans**

Transplant rejection

(**xenotransplant**; **pancreatic islet xenograft**
 tolerance after short-term costimulation blockade is assocd. with
 increased CD4+ T cell apoptosis but not immune deviation)

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L65 ANSWER 14 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:264346 HCAPLUS

DN 133:176095

TI Damage to porcine **islets** of **Langerhans** after exposure to human blood in vitro, or after intraportal **transplantation** to cynomolgus monkeys. Protective effects of sCR1 and **heparin**

AU **Bennet, William**; Sundberg, Berit; Lundgren, Torbjorn; Tibell, Annika; Groth, Carl-Gustav; Richards, Andrew; White, David J.; Elgue, Graciela; **Larsson, Rolf**; **Nilsson, Bo**; **Korsgren, Olle**

CS Department of Transplantation Surgery, Karolinska Institutet, Huddinge Hospital, Huddinge, S-141 86, Swed.

SO Transplantation (2000), 69(5), 711-719

CODEN: TRPLAU; ISSN: 0041-1337

PB Lippincott Williams & Wilkins

DT Journal

LA English

CC 15-8 (Immunochemistry)

AB Porcine **islets** offer an attractive alternative to human **islets** in clin. **islet transplantation**. The preferred method of **islet transplantation** is intraportal injection into the liver. The authors have recently shown, both in vitro with human **islets** and in vivo with porcine **islets**, that **islets** exposed to allogeneic blood trigger an injurious inflammatory reaction characterized by activation of both coagulation and the complement systems. The authors have now tested whether a similar reaction is triggered when xenogeneic porcine **islets** are exposed to human blood in vitro and after intraportal **transplantation** into primates. Furthermore, the authors investigated the effect of inhibiting the complement and coagulation systems. **Islets** isolated from adult and fetal porcine pancreas were perfused with fresh human blood in surface heparinized PVC tubings for 5-60 min. Blood cell counts and parameters related to coagulation and the complement system were analyzed, and **islets** were retrieved after the perfusion was examd. by immunohistochem. method. **Heparin** and sol. complement receptor 1 (sCR1; TP10, 100 .mu.g/mL) were added to the system in some expts. Furthermore, adult porcine **islets** were **transplanted** intraportally into untreated and sCR1- (40 mg/kg BW i.v.) treated cynomolgus monkeys, and plasma **insulin** concn. was monitored during 60 min. after **transplantation**. Porcine **islets** perfused with human blood triggered an immediate inflammatory reaction, characterized by a rapid consumption and activation of platelets, consumption of neutrophils and monocytes, activation of the coagulation and complement systems, and release of large amts. of **insulin**. **Islet** morphol. anal. revealed damaged **islets** embedded in clots and infiltrated with CD11+ leukocytes. C3a and C5b-9 was deposited on the **islet** surface, but human Ig was not. Complement inhibition with sCR1 reduced **insulin** release significantly. Intraportal **islet transplantation** into untreated cynomolgus monkeys resulted in a marked and rapid increase in plasma **insulin** concn. indicative of **islet** damage. Pretreatment of the monkeys with sCR1 resulted in significantly less **insulin** release than in untreated control monkeys. Exposure of isolated xenogeneic **islets** of **Langerhans** to blood, both in vitro and in vivo, resulted in acute **islet** damage. Complement and platelets seem to have a central role in the reactions described. Strategies to efficiently inhibit these reactions will be crucial for clin. intraportal **islet xenotransplantation** to be successful.

ST **Langerhans islet xenotransplant** inflammation

complement platelet; insulin heparin
Langerhans islet xenotransplant; complement
 receptor 1 **Langerhans islet xenotransplant**;
 neutrophil monocyte **Langerhans islet**
xenotransplant

- IT CD antigens
 CD antigens
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
 BIOL (Biological study); OCCU (Occurrence)
 (CD11; CD11+ leukocytes infiltration into **Langerhans**
islets after **xenotransplantation**)
- IT Leukocyte
 (CD11+ leukocytes infiltration into **Langerhans islets**
 after **xenotransplantation**)
- IT Blood-coagulation factors
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological
 process); BSU (Biological study, unclassified); BIOL (Biological study);
 PROC (Process)
 (activation of coagulation system after porcine **Langerhans**
islets xenotransplantation)
- IT Lymphocyte
 (activation of lymphocytes after porcine **Langerhans**
islets xenotransplantation)
- IT Monocyte
 (activation of monocytes after porcine **Langerhans**
islets xenotransplantation)
- IT Neutrophil
 (activation of neutrophils after porcine **Langerhans**
islets xenotransplantation)
- IT Platelet (blood)
 (activation of platelets after porcine **Langerhans**
islets xenotransplantation)
- IT Inflammation
 (activation of platelets, neutrophils, and monocytes, the coagulation
 and complement systems, and **insulin** release after porcine
Langerhans islets xenotransplantation)
- IT Integrins
 Integrins
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
 BIOL (Biological study); OCCU (Occurrence)
 (antigens CD11; CD11+ leukocytes infiltration into **Langerhans**
islets after **xenotransplantation**)
- IT Complement receptors
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); BIOL (Biological study)
 (type 1; protective effects of sCR1 and **heparin** against
 damage of porcine **Langerhans islets** after
xenotransplantation)
- IT Transplant and Transplantation
Transplant and Transplantation
 (**xenotransplant**, **islet** of
Langerhans; protective effects of sCR1 and **heparin**
 against damage of porcine **Langerhans islets** after
xenotransplantation)
- IT Pancreatic islet of Langerhans
 (**xenotransplant**; protective effects of sCR1 and
heparin against damage of porcine **Langerhans**
islets after **xenotransplantation**)
- IT Thromboglobulins
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological
 process); BSU (Biological study, unclassified); BIOL (Biological study);
 PROC (Process)
 (.beta.-; activation of coagulation system after porcine

- Langerhans islets xenotransplantation)**
- IT 9003-99-0, Myeloperoxidase
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (activation of myeloperoxidase after porcine **Langerhans islets xenotransplantation)**
- IT 80295-42-7, Complement C3a 82986-89-8, Complement C5b-9
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (activation of the complement system after porcine **Langerhans islets xenotransplantation)**
- IT 9000-94-6, Antithrombin
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (complex with FXIIa, FXIa, **thrombin**; activation of coagulation system after porcine **Langerhans islets xenotransplantation)**
- IT 9002-04-4, **Thrombin** 37203-61-5, Factor XIa 37203-62-6, Factor XIIa
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (complex with **antithrombin**; activation of coagulation system after porcine **Langerhans islets xenotransplantation)**
- IT 9004-10-8, **Insulin**, biological studies
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (**insulin** secretion after porcine **Langerhans islets** after **xenotransplantation**)
- IT 9005-49-6, **Heparin**, biological studies
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (protective effects of sCR1 and **heparin** against damage of porcine **Langerhans islets** after **xenotransplantation**)

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L65 ANSWER 15 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:84982 HCAPLUS

DN 132:133245

TI An internal ribosome entry site from the X-linked inhibitor of apoptosis gene and its uses

IN Korneluk, Robert G.; Holcik, Martin; Liston, Peter

PA University of Ottawa, Can.

SO PCT Int. Appl., 87 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C12N015-12

ICS C12N005-10; C07K014-47; C12Q001-68; G01N033-50

CC 3-5 (Biochemical Genetics)

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000005366	A2	20000203	WO 1999-IB1415	19990722 <--
	WO 2000005366	A3	20000615		
	W: CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6159709	A	20001212	US 1998-121979	19980724 <--
	US 6171821	B1	20010109	US 1999-332319	19990614 <--
	CA 2336707	AA	20000203	CA 1999-2336707	19990722 <--
	EP 1100900	A2	20010523	EP 1999-935002	19990722 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	US 1998-121979	A2	19980724	<--	
	US 1999-332319	A2	19990614	<--	
	WO 1999-IB1415	W	19990722	<--	

AB A novel internal ribosome entry site (IRES) sequence from the X-linked inhibitor of apoptosis (XIAP) gene is identified and characterized. The invention also features methods for using the XIAP IRES to increase cap-independent translation of polypeptide coding sequences linked to the XIAP IRES, and methods for isolating compds. that modulate cap-independent translation. The IRES was identified in the very long 5'-UTR of the XIAP gene by function. Cap-independent initiation of translation from the IRES was demonstrated by resistance of expression of the downstream gene to

inhibition by poliovirus protease 2A. The IRES could also mediate translation during serum starvation and the IRES also improved XIAP-mediated inhibition of apoptosis during serum starvation. The La autoantigen was shown to be involved in translation from the IRES.

- ST IRES gene XIAP apoptosis regulation starvation
- IT Proteins, specific or class
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (Bad, induction of synthesis of, in induction of apoptosis; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Proteins, specific or class
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (Bax, induction of synthesis of, in induction of apoptosis; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Proteins, specific or class
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (Bcl-x, L1, regulation of levels of; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Proteins, specific or class
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (FADD (Fas-assocd. death domain), induction of synthesis of, in induction of apoptosis; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Genetic element
 - RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
 - (IRES (internal ribosomal entry site) element; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Mouse (Mus musculus)
 - (IRES elements of XIAP genes of human and; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Translation, genetic
 - Translation initiation
 - (IRES for cap-independent translation of reporter gene in screening for inhibitors of; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Apoptosis
 - (IRES of XIAP gene in control of; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Antigens
 - RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 - (La (lymphocyte activation), in cap-independent gene expression for IRES; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Proteins, specific or class
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (TRADD (tumor necrosis factor receptor-assocd. death domain), induction of synthesis of, in induction of apoptosis; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Proteins, specific or class
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (XAF, induction of synthesis of, in induction of apoptosis; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Gene, animal
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (XIAP; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Proteins, specific or class
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)

- (apoptosis-regulating, XIAP, NAIP, TIAP, HIAP1, HIAP2, regulation of levels of; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Proteins, specific or class
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (bcl-2, regulation of levels of; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Neurotrophic factors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (brain-derived, regulation of levels of; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Astrocyte
 Myoblast
 Oligodendrocyte
Pancreatic islet of Langerhans
 (control of apoptosis in treatment of diseases affecting; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Autoimmune disease
Transplant rejection
 (control of apoptosis in treatment of; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Disease, animal
 (degenerative, control of apoptosis in treatment of; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Muscle
 (fiber, control of apoptosis in treatment of diseases affecting; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Hair
 Ovary
 (follicle, control of apoptosis in treatment of diseases affecting; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Drug screening
 (for translation inhibitors; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Proteins, specific or class
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (gene VHL, induction of synthesis of, in induction of apoptosis; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Neurotrophic factors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (glia-derived, regulation of levels of; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Brain
 Heart
 (induction of anti-apoptosis protein in treatment of hypoxia in; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Hypoxia, animal
 (induction of anti-apoptosis protein in treatment of; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT p53 (protein)
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (induction of synthesis of, in induction of apoptosis; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)
- IT Heart
 (myocyte, control of apoptosis in treatment of diseases affecting; internal ribosome entry site from X-linked inhibitor of apoptosis gene and its uses)

IT Nerve
(neuron, control of apoptosis in treatment of diseases affecting;
internal ribosome entry site from X-linked inhibitor of apoptosis gene
and its uses)

IT DNA sequences
(of IRES elements of XIAP genes of human and mouse; internal ribosome
entry site from X-linked inhibitor of apoptosis gene and its uses)

IT Eye
(photoreceptor, control of apoptosis in treatment of diseases
affecting; internal ribosome entry site from X-linked inhibitor of
apoptosis gene and its uses)

IT Platelet-derived growth factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(regulation of levels of .beta. subunit; internal ribosome entry site
from X-linked inhibitor of apoptosis gene and its uses)

IT Ciliary neurotrophic factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(regulation of levels of; internal ribosome entry site from X-linked
inhibitor of apoptosis gene and its uses)

IT Antitumor agents
(screening for translation inhibitors for use as; internal ribosome
entry site from X-linked inhibitor of apoptosis gene and its uses)

IT 127464-60-2, Vascular endothelial growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IRES of gene for, in reporter constructs for screening for translation
inhibitors; internal ribosome entry site from X-linked inhibitor of
apoptosis gene and its uses)

IT 122191-40-6, Caspase 1 169592-56-7, Caspase 3 179241-78-2, Caspase 8
180189-96-2, Caspase 9 182372-14-1, Caspase 2 182372-15-2, Caspase 6
182762-08-9, Caspase 4 189088-85-5, Caspase 10 189258-14-8, Caspase 7
192465-11-5, Caspase 5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(induction of synthesis of, in induction of apoptosis; internal
ribosome entry site from X-linked inhibitor of apoptosis gene and its
uses)

IT **106096-93-9**, Basic fibroblast growth factor
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(induction of synthesis of, in treatment of hypoxic stress; internal
ribosome entry site from X-linked inhibitor of apoptosis gene and its
uses)

IT 256436-51-8 256436-52-9 256436-53-0 256436-54-1 256436-55-2
256436-56-3 256436-57-4 256436-58-5 256436-59-6 256436-60-9
256436-61-0 256436-62-1
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP
(Properties); THU (Therapeutic use); BIOL (Biological study); PROC
(Process); USES (Uses)
(nucleotide sequence; internal ribosome entry site from X-linked
inhibitor of apoptosis gene and its uses)

IT **9004-10-8, Insulin**, biological studies 9014-42-0,
Thrombopoietin 11096-26-7, Erythropoietin **67763-97-7**, IGF-2
130939-66-1, Neurotrophic factor 3 143375-33-1, Neurotrophic factor 4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(regulation of levels of; internal ribosome entry site from X-linked
inhibitor of apoptosis gene and its uses)

IT 256438-37-6, 1: PN: WO0005366 SEQID: 1 unclaimed DNA 256438-38-7, 2: PN:
WO0005366 SEQID: 2 unclaimed DNA 256438-39-8, 3: PN: WO0005366 SEQID: 3
unclaimed DNA 256438-41-2, 5: PN: WO0005366 SEQID: 5 unclaimed DNA
256438-42-3, 7: PN: WO0005366 SEQID: 7 unclaimed DNA 256438-43-4, 9: PN:
WO0005366 SEQID: 9 unclaimed DNA 256438-44-5 256438-45-6 256438-46-7
256438-47-8 256438-48-9 256438-49-0 256438-50-3 256438-51-4
256438-52-5
RL: PRP (Properties)
(unclaimed nucleotide sequence; internal ribosome entry site from the

IT X-linked inhibitor of apoptosis gene and its uses)
 256438-40-1
 RL: PRP (Properties)
 (unclaimed protein sequence; internal ribosome entry site from the
 X-linked inhibitor of apoptosis gene and its uses)

L65 ANSWER 16 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:53841 HCAPLUS

DN 132:90359

TI Polar amino acids in medium and hydrogel matrix for long-term
 proliferation of cells

IN Usala, Anton-Lewis; Klann, Richard Chris

PA Encelle, Inc., USA

SO PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C12N005-02

ICS C12N005-06

CC 9-11 (Biochemical Methods)

Section cross-reference(s): 63

FAN.CNT 12

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000002999	A2	20000120	WO 1999-US15464	19990709 <--
	WO 2000002999	A3	20000420		
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	US 6231881	B1	20010515	US 1998-113437	19980710 <--
	CA 2332701	AA	20000120	CA 1999-2332701	19990709 <--
	AU 9949772	A1	20000201	AU 1999-49772	19990709 <--
	EP 1098959	A2	20010516	EP 1999-933791	19990709 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
	JP 2002520013	T2	20020709	JP 2000-559221	19990709 <--
PRAI	US 1998-113437	A	19980710	<--	
	US 1992-841973	B2	19920224	<--	
	US 1994-300429	B2	19940902	<--	
	US 1995-568482	A2	19951207	<--	
	WO 1999-US15464	W	19990709	<--	

AB A cell culture medium and hydrogel matrix for long term storage and proliferation of cells is provided. The cell culture medium and hydrogel matrix may include an effective amt. of polar amino acids, the polar amino acids selected from the group consisting of arginine, lysine, histidine, glutamic acid, and aspartic acid. One embodiment of the cell culture medium comprises about 5 to about 150 mM of polar amino acids. The hydrogel matrix comprises about 3 to about 150 mM of polar amino acids. L-arginine and L-glutamic acid are preferably supplemented in the cell culture medium. L-arginine, L-lysine, and L-glutamic acid are preferably supplemented in the hydrogel matrix. A method of maintaining viability and functioning of a **transplant** is also provided. The method of maintaining viability of a **transplant** includes encapsulating the cells in a hydrogel matrix and injecting the encapsulated cells into the host organism. The matrix of the present invention may also be used to promote vascularization in a **transplant** site prior to injection of cells. Digested unpurified and purified porcine pancreatic tissue

samples were placed in a matrix contg. 5 mM lysine, 5 mM arginine, and 10 mM glutamic acid in addn. to 180 .mu.M cysteine and stored at -20.degree.. Inspection of the cells indicated appropriate morphol. of both the islet tissue and digestive acinar cells in an unpurified prepn. that was frozen for 6 wk.

- ST polar amino acid culture medium hydrogel matrix; **transplant**
hydrogel matrix encapsulation cell; pancreas islet acinar cell
preservation **insulin**
- IT Liver
(Kupffer cell; polar amino acids in medium and hydrogel matrix for
long-term proliferation of cells)
- IT Pancreas
(acinar cell; polar amino acids in medium and hydrogel matrix for
long-term proliferation of cells)
- IT Blood serum
(as nutrient source; polar amino acids in medium and hydrogel matrix
for long-term proliferation of cells)
- IT Albumins, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(as nutrient source; polar amino acids in medium and hydrogel matrix
for long-term proliferation of cells)
- IT Brain
Epithelium
Heart
Kidney
Liver
Lung
Thymus gland
Thyroid gland
(cells of; polar amino acids in medium and hydrogel matrix for
long-term proliferation of cells)
- IT Enzymes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(culture medium for cell protection during tissue digestion with; polar
amino acids in medium and hydrogel matrix for long-term proliferation
of cells)
- IT Chelating agents
(divalent, hydrogel matrix contg.; polar amino acids in medium and
hydrogel matrix for long-term proliferation of cells)
- IT Liver
(hepatocyte; polar amino acids in medium and hydrogel matrix for
long-term proliferation of cells)
- IT Cryoprotectants
(hydrogel matrix contg.; polar amino acids in medium and hydrogel
matrix for long-term proliferation of cells)
- IT Collagens, biological studies
RL: BUU (Biological use, unclassified); DEV (Device component use); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrogel matrix contg.; polar amino acids in medium and hydrogel
matrix for long-term proliferation of cells)
- IT Gelatins, biological studies
RL: BUU (Biological use, unclassified); DEV (Device component use); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrogel matrix of; polar amino acids in medium and hydrogel matrix
for long-term proliferation of cells)
- IT Cell
(long-term storage of; polar amino acids in medium and hydrogel matrix
for long-term proliferation of cells)
- IT **Transplant and Transplantation**
(matrix-encapsulated cells for; polar amino acids in medium and
hydrogel matrix for long-term proliferation of cells)

- IT Nerve
(neuron; polar amino acids in medium and hydrogel matrix for long-term proliferation of cells)
- IT Animal tissue culture
Cell proliferation
Cryopreservation
Culture media
Erythrocyte
Hydrogels
Matrix media
Nutrients
Pancreatic islet of Langerhans
(polar amino acids in medium and hydrogel matrix for long-term proliferation of cells)
- IT Amino acids, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polar; polar amino acids in medium and hydrogel matrix for long-term proliferation of cells)
- IT Oxides (inorganic), biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(superoxides, inhibitor of; polar amino acids in medium and hydrogel matrix for long-term proliferation of cells)
- IT 9004-54-0, Dextran, biological studies
RL: BUU (Biological use, unclassified); DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as cryoprotectant, hydrogel matrix contg.; polar amino acids in medium and hydrogel matrix for long-term proliferation of cells)
- IT 52-90-4, L-Cysteine, biological studies 56-89-3, Cystine, biological studies 74-79-3D, L-Arginine, analogs, biological studies 79-17-4, Aminoguanidine **9005-49-6, Heparin**, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(as nitric oxide inhibitor; polar amino acids in medium and hydrogel matrix for long-term proliferation of cells)
- IT 60-00-4, EDTA, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(as superoxide inhibitor; polar amino acids in medium and hydrogel matrix for long-term proliferation of cells)
- IT 10102-43-9, Nitric oxide, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(inhibitor of; polar amino acids in medium and hydrogel matrix for long-term proliferation of cells)
- IT **9004-10-8, Insulin**, biological studies
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(matrix encapsulation of acinar and islet cells for **transplantation** and prodn. of; polar amino acids in medium and hydrogel matrix for long-term proliferation of cells)
- IT 56-84-8, Aspartic acid, biological studies 56-86-0, Glutamic acid, biological studies 56-87-1, Lysine, biological studies 71-00-1, Histidine, biological studies 74-79-3, Arginine, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polar amino acids in medium and hydrogel matrix for long-term proliferation of cells)

L65 ANSWER 17 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:53454 HCAPLUS

DN 132:98151

TI Pharmaceutical hydrogels for obscuring immune recognition of a

transplant

IN Usala, Anton-Lewis; Klann, Richard Chris

PA Encelle, Inc., USA

SO PCT Int. Appl., 30 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61L033-00

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

FAN.CNT 12

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000002600	A1	20000120	WO 1999-US15465	19990709 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6231881	B1	20010515	US 1998-113437	19980710 <--
US 6352707	B1	20020305	US 1999-346212	19990701 <--
CA 2337047	AA	20000120	CA 1999-2337047	19990709 <--
AU 9949773	A1	20000201	AU 1999-49773	19990709 <--
EP 1096962	A1	20010509	EP 1999-933792	19990709 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRAI US 1998-113437 A 19980710 <--
 US 1999-346212 A 19990701 <--
 US 1992-841973 B2 19920224 <--
 US 1994-300429 B2 19940902 <--
 US 1995-568482 A2 19951207 <--
 WO 1999-US15465 W 19990709 <--

AB A method of obscuring immune recognition of a **transplant** by a host mammal is provided by encapsulating tissue suitable for use in a **transplant** within a hydrogel matrix, wherein the hydrogel matrix comprises gelatin, dextran, at least one nitric oxide inhibitor, and an effective amt. of polar amino acids. The matrix binds to the cell surface proteins of the tissue and obscures recognition of the tissue by high affinity antibodies produced by the recipient of the **transplant**. A hydrogel was prep'd. from a mixt. of amino acids, albumin, dextran, EDTA, and collagen in Medium 199 contg. porcine pancreatic cells. The hydrogel was injected to a diabetic dog over a 19 wk period. The amt. of **insulin** required to maintain the target glucose value (180 mg/dL or less) decreased after the injection and the av. glucose level of the dog decreased.

ST pharmaceutical hydrogel immune recognition **transplant**

IT Pancreas

(acinus, cells; pharmaceutical hydrogels for obscuring immune recognition of **transplant**)

IT Proteins, specific or class

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cell surface-assocd.; pharmaceutical hydrogels for obscuring immune recognition of **transplant**)

IT Brain

Heart

Kidney

Liver

Lung

Pancreatic islet of Langerhans

Thyme (Thymus)
 Thyroid gland
 (cells; pharmaceutical hydrogels for obscuring immune recognition of
 transplant)

IT Drug delivery systems
 (hydrogels; pharmaceutical hydrogels for obscuring immune recognition
 of **transplant**)

IT Drug delivery systems
 (implants; pharmaceutical hydrogels for obscuring immune recognition of
 transplant)

IT Drug delivery systems
 (injections, i.m.; pharmaceutical hydrogels for obscuring immune
 recognition of **transplant**)

IT Drug delivery systems
 (injections, i.p.; pharmaceutical hydrogels for obscuring immune
 recognition of **transplant**)

IT Drug delivery systems
 (injections, i.v.; pharmaceutical hydrogels for obscuring immune
 recognition of **transplant**)

IT Drug delivery systems
 (injections, s.c.; pharmaceutical hydrogels for obscuring immune
 recognition of **transplant**)

IT Drug delivery systems
 (microcapsules; pharmaceutical hydrogels for obscuring immune
 recognition of **transplant**)

IT Immunity
 (pharmaceutical hydrogels for obscuring immune recognition of
 transplant)

IT Collagens, biological studies
 Gelatins, biological studies
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (pharmaceutical hydrogels for obscuring immune recognition of
 transplant)

IT Amino acids, biological studies
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (polar; pharmaceutical hydrogels for obscuring immune recognition of
 transplant)

IT 10102-43-9, Nitric oxide, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitor; pharmaceutical hydrogels for obscuring immune recognition
 of **transplant**)

IT 56-84-8, L Aspartic acid, biological studies 56-86-0, L Glutamic acid,
 biological studies 56-87-1, L Lysine, biological studies 60-00-4,
 EDTA, biological studies 71-00-1, L Histidine, biological studies
 74-79-3, L Arginine, biological studies 79-17-4, Aminoguanidine
 9004-54-0, Dextran,, biological studies **9005-49-6,**
Heparin, biological studies
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (pharmaceutical hydrogels for obscuring immune recognition of
 transplant)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
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 (2) Encelle Inc; WO 9720569 A 1997 HCAPLUS
 (3) Lifecell Corp; EP 0564786 A 1993 HCAPLUS

L65 ANSWER 18 OF 49 HCAPLUS COPYRIGHT 2002 ACS
 AN 1999:769132 HCAPLUS
 DN 132:62561
 TI Maintenance of beta-cell function and survival following islet isolation
 requires re-establishment of the islet-matrix relationship
 AU Wang, R. N.; Rosenberg, L.
 CS Department of Surgery, McGill University, Montreal, QC, Can.

SO Journal of Endocrinology (1999), 163(2), 181-190
 CODEN: JOENAK; ISSN: 0022-0795

PB Society for Endocrinology

DT Journal

LA English

CC 14-8 (Mammalian Pathological Biochemistry)
 Section cross-reference(s): 2

AB Islet **transplantation** is assocd. with a high rate of early **graft** failure, a problem that remains poorly understood. It is probable that the destruction of the islet microenvironment and loss of tropic support that occur during isolation lead to compromised survival. The purpose of this study was to det. the role of matrix-integrin interactions on beta-cell survival and function following islet isolation. Canine islets were obtained by conventional methods. Immediately after isolation, the peri-insular basement membrane (BM) was absent. The ability of islets maintained in suspension culture to attach to a collagen matrix declined progressively over 6 days. Attachment could be blocked by an **arginine-glycine-aspartate** (RGD) motif-presenting synthetic peptide, thereby implicating an integrin-mediated process. Characterization of cell surface integrins by immunocytochem. (ICC) demonstrated that the expression of integrins .alpha.3, .alpha.5 and .alpha.V diminished during the culture period. This change was coincident with both a decrease in beta-cell function (proinsulin gene expression, islet **insulin** content and stimulated **insulin** release) and a rise in beta-cell death from apoptosis, as detd. by in situ cell death detection (TUNEL) assay. These adverse events were prevented or delayed by exposure of islets to matrix proteins. In conclusion, routine islet isolation disrupts the cell-matrix relationship leading to a variety of structural and functional abnormalities, including apoptotic cell death. These alterations can be diminished by restoration of a culture microenvironment that includes matrix proteins.

ST pancreatic beta cell isolation survival matrix

IT Collagens, biological studies
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (culture matrix; pancreatic .beta.-cell function maintenance and survival following islet isolation requires re-establishment of islet-matrix relationship)

IT Apoptosis
 Basement membrane
 Cell membrane
 Extracellular matrix
 Organ preservation
Transplant and Transplantation
 (pancreatic .beta.-cell function maintenance and survival following islet isolation requires re-establishment of islet-matrix relationship)

IT Animal tissue culture
 (suspension; pancreatic .beta.-cell function maintenance and survival following islet isolation requires re-establishment of islet-matrix relationship)

IT Integrins
 RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
 (.alpha.v; pancreatic .beta.-cell function maintenance and survival following islet isolation requires re-establishment of islet-matrix relationship)

IT Integrins
 RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
 (.alpha.3; pancreatic .beta.-cell function maintenance and survival following islet isolation requires re-establishment of islet-matrix relationship)

- IT Integrins
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(.alpha.5; pancreatic .beta.-cell function maintenance and survival following islet isolation requires re-establishment of islet-matrix relationship)
- IT **Pancreatic islet of Langerhans**
(.beta.-cell; pancreatic .beta.-cell function maintenance and survival following islet isolation requires re-establishment of islet-matrix relationship)
- IT **9004-10-8, Insulin**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pancreatic .beta.-cell function maintenance and survival following islet isolation requires re-establishment of islet-matrix relationship)
- IT **9035-68-1, Proinsulin**
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(pancreatic .beta.-cell function maintenance and survival following islet isolation requires re-establishment of islet-matrix relationship)
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L65 ANSWER 19 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:736930 HCAPLUS

DN 131:350265

TI Antibodies to CD23

IN Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean

PA Glaxo Group Limited, UK

SO PCT Int. Appl., 81 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C12N015-13

ICS C07K016-28; A61K039-395; C12N015-62

CC 15-3 (Immunochemistry)

Section cross-reference(s): 3

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9958679	A1	19991118	WO 1999-GB1434	19990507	<--
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2328606	AA	19991118	CA 1999-2328606	19990507	<--
	AU 9938367	A1	19991129	AU 1999-38367	19990507	<--
	BR 9910327	A	20010130	BR 1999-10327	19990507	<--
	EP 1076701	A1	20010221	EP 1999-920991	19990507	<--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NO 2000005632	A	20010108	NO 2000-5632	20001108	<--
PRAI	GB 1998-9839	A	19980509			<--
	WO 1999-GB1434	W	19990507			<--

AB The authors disclose the prepn. and characterization of murine **monoclonal** and humanized **antibodies** which bind to the CD23 (**Fc**.epsilon.RII receptor) antigen. In one example, humanized IgG1, with mutations to eliminate Clq and **Fc** binding, was shown to bind to CD23 with assocn. rates of the order of 1.5-1.85 x 10⁶ M⁻¹ s⁻¹ and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the treatment of autoimmune and inflammatory disorders.

ST antibody CD23 antigen; **FcepsilonRII** receptor antibody

IT Antitumor agents
 (B-cell leukemia; anti-CD23 antibodies as)

IT Antitumor agents
 (B-cell lymphoma; anti-CD23 antibodies as)

IT Intestine, disease
 (Crohn's; anti-CD23 antibodies in treatment of)

IT **Immunoglobulin receptors**

- RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(IgE type II, sol.; prepn. and characterization of antibodies to)
- IT **Immunoglobulin receptors**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(IgE type II; prepn. and characterization of antibodies to)
- IT Allergy inhibitors
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antidiabetic agents
(anti-CD23 antibodies as)
- IT Dermatitis
Eczema
Psoriasis
Sjogren's syndrome
Urticaria
(anti-CD23 antibodies in treatment of)
- IT Thyroid gland, disease
(autoimmune thyroiditis; anti-CD23 antibodies in treatment of)
- IT Bronchi
(bronchitis; anti-CD23 antibodies in treatment of)
- IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chimeric; to CD23 on hematopoietic cells)
- IT Lung, disease
(chronic obstructive; anti-CD23 antibodies in treatment of)
- IT Kidney, disease
(glomerulonephritis; anti-CD23 antibodies in treatment of)
- IT **Transplant and Transplantation**
(**graft-vs.-host reaction**;
anti-CD23 antibodies in treatment of)
- IT **Immunoglobulins**
RL: PRP (Properties)
(heavy chains, CDR; of antibodies to CD23)
- IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(humanized; to CD23 on hematopoietic cells)
- IT Intestine, disease
(inflammatory; anti-CD23 antibodies in treatment of)
- IT **Pancreatic islet of Langerhans**
(**insulinitis**; anti-CD23 antibodies in treatment of)
- IT **Immunoglobulins**
RL: PRP (Properties)
(light chains, CDR; of antibodies to CD23)
- IT Kidney, disease
(nephrotic syndrome; anti-CD23 antibodies in treatment of)
- IT Protein sequences
cDNA sequences
(of antibody fragments to CD23)
- IT Blood cell
(prepn. and characterization of antibodies to CD23 of)
- IT Nose
(rhinitis; anti-CD23 antibodies in treatment of)
- IT Lupus erythematosus
(systemic; anti-CD23 antibodies in treatment of)
- IT Multiple sclerosis
(therapeutic agents; anti-CD23 antibodies as)

IT Antibodies
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (to CD23 on hematopoietic cells)

IT Intestine, disease
 (ulcerative colitis; anti-CD23 antibodies in treatment of)

IT Eye, disease
 (uveitis; anti-CD23 antibodies in treatment of)

IT 250332-00-4 250332-01-5 250332-02-6 250332-03-7
 RL: PRP (Properties)
 (amino acid sequence; anti-CD23 antibodies as)

IT 250332-04-8 250332-05-9 250332-06-0 250332-07-1
 RL: PRP (Properties)
 (nucleotide sequence; anti-CD23 antibodies as)

IT 175175-73-2 201468-24-8, LMSTRAS 250143-97-6, RSSKSLLYKDGKTYLN
 250143-98-7, QQLVEYPFT 250143-99-8, GYWMS 250144-00-4,
 EIRLKSDNYATHYAESVKG
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
 (of antibodies to CD23)

IT 250242-61-6, CGCTCGAGTAAGAGTCTCCTGTATAAGGATGGGAAGACATACTTGAAT
 250242-63-8, TTGATGTCCACCCGGGCATCA 250242-65-0,
 CAACAGCTGGTAGAGTATCCATTACG 250242-67-2, GGCTACTGGATGTCC 250242-69-4,
 GAAATTAGATTGAAATCTGATAATTATGCAACACATTATGCGGAGTCT 250242-71-8, TTCATAGAC
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
 BIOL (Biological study); OCCU (Occurrence)
 (of nucleic acid encoding antibodies to CD23)

IT 162565-25-5, GenBank A18463 162565-71-1, GenBank A18479 162565-72-2,
 GenBank A18480 250332-75-3 250382-76-4 250382-77-5 250382-78-6
 250382-79-7 250382-81-1 250382-82-2 250382-83-3 250382-84-4
 250382-85-5 250382-88-8 250382-89-9 250382-90-2 250382-91-3
 250382-92-4 250382-93-5 250382-94-6 250382-95-7 250382-96-8
 RL: PRP (Properties)
 (unclaimed nucleotide sequence; antibodies to CD23)

IT 247166-37-6 250253-00-0 250253-04-4 250253-05-5 250253-06-6
 250253-07-7
 RL: PRP (Properties)
 (unclaimed sequence; antibodies to CD23)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L65 ANSWER 20 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:672498 HCAPLUS

DN 131:291339

TI Vascularizable biomaterials for creation of three-dimensional tissues

IN Halberstadt, Craig R.; Holder, Walter D., Jr.

PA Charlotte-Mecklenberg Hospital Authority, USA

SO PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A01N001-02

ICS C12P019-34; C12M003-00

CC 63-7 (Pharmaceuticals)

Section cross-reference(s): 9, 14

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9952356	A1	19991021	WO 1999-US7816	19990409 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2330104	AA	19991021	CA 1999-2330104	19990409 <--
	AU 9935520	A1	19991101	AU 1999-35520	19990409 <--
	EP 1069822	A1	20010124	EP 1999-917384	19990409 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002511284	T2	20020416	JP 2000-542979	19990409 <--
PRAI	US 1998-58619	A2	19980409 <--		
	WO 1999-US7816	W	19990409 <--		
AB	A method of providing a vascularized, three-dimensional tissue in a living subject is disclosed. The method includes the steps of (a) creating, from a biocompatible material capable of supporting cell adhesion, growth, and migration, a porous construct contg. cells to be transplanted , and (b) delivering the construct into an area of interest in the living subject to form a vascularized three-dimensional tissue. The preferred construct has a dimension in which it is about 50 .mu.mm to about 500 .mu.mm from the outermost surface to the center of the construct. The preferred construct also has an interconnected porous structure having a pore size of from about 10 .mu.mm to no greater than 300 .mu.mm. The cells within the preferred construct are no greater than 250 .mu.mm from an outer surface of the construct.				
ST	artificial organ tissue vascularization transplant				
IT	Testis (Sertoli cell, culture of; vascularizable biomaterials for creation of three-dimensional tissues)				
IT	Adipose tissue (adipocyte, culture of; vascularizable biomaterials for creation of three-dimensional tissues)				
IT	Transplant and Transplantation (allotransplant ; vascularizable biomaterials for creation of three-dimensional tissues)				
IT	Artery (arteriole, of biocompatible pouch; vascularizable biomaterials for creation of three-dimensional tissues)				
IT	Animal tissue Organ, animal (artificial; vascularizable biomaterials for creation of three-dimensional tissues)				
IT	Transplant and Transplantation (autotransplant ; vascularizable biomaterials for creation of three-dimensional tissues)				
IT	Adrenal gland Chondrocyte Fibroblast Muscle Osteocyte Pancreatic islet of Langerhans (culture of; vascularizable biomaterials for creation of three-dimensional tissues)				
IT	Blood vessel (endothelium, culture of; vascularizable biomaterials for creation of three-dimensional tissues)				

IT Growth factors, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(epithelial cell growth factors; vascularizable biomaterials for creation of three-dimensional tissues)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(extracellular matrix-assocd.; vascularizable biomaterials for creation of three-dimensional tissues)

IT Liver
(hepatocyte, culture of; vascularizable biomaterials for creation of three-dimensional tissues)

IT Drug delivery systems
(hydrogels; vascularizable biomaterials for creation of three-dimensional tissues)

IT Polyesters, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(hydroxycarboxylic acid-based; vascularizable biomaterials for creation of three-dimensional tissues)

IT Prosthetic materials and Prosthetics
(implants; vascularizable biomaterials for creation of three-dimensional tissues)

IT Drug delivery systems
(injections; vascularizable biomaterials for creation of three-dimensional tissues)

IT Muscle
(morphogenic factor; vascularizable biomaterials for creation of three-dimensional tissues)

IT Heart
(myocyte, culture of; vascularizable biomaterials for creation of three-dimensional tissues)

IT Nerve
(neuron, culture of; vascularizable biomaterials for creation of three-dimensional tissues)

IT Muscle
(smooth, culture of; vascularizable biomaterials for creation of three-dimensional tissues)

IT Animal tissue
(soft, defects in; vascularizable biomaterials for creation of three-dimensional tissues)

IT Cell
(stem, culture of; vascularizable biomaterials for creation of three-dimensional tissues)

IT Thyroid gland
(thyrocyte, culture of; vascularizable biomaterials for creation of three-dimensional tissues)

IT Kidney
(tubule, culture of; vascularizable biomaterials for creation of three-dimensional tissues)

IT Collagens, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(type I; vascularizable biomaterials for creation of three-dimensional tissues)

IT Angiogenesis
Animal tissue culture
Biocompatibility

Biological materials

Cell adhesion

Cell migration

Particle size

Porous materials

Resorption, animal

(vascularizable biomaterials for creation of three-dimensional tissues)

IT Adhesins

Growth factors, animal

Hormones, animal, biological studies

Platelet-derived growth factors

Transforming growth factors

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(vascularizable biomaterials for creation of three-dimensional tissues)

IT Biopolymers

Collagens, biological studies

Fibronectins

Fluoropolymers, biological studies

Laminins

Polyamides, biological studies

Polycarbonates, biological studies

Polyesters, biological studies

Polyoxyalkylenes, biological studies

Polyphosphazenes

Polyurethanes, biological studies

Vitronectin

RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(vascularizable biomaterials for creation of three-dimensional tissues)

IT Vein

(venule, of biocompatible pouch; vascularizable biomaterials for creation of three-dimensional tissues)

IT **Transplant and Transplantation**

(**xenotransplant**; vascularizable biomaterials for creation of three-dimensional tissues)

IT 9061-61-4, Nerve growth factor 99896-85-2 **106096-92-8**, Acidic

fibroblast growth factor **106096-93-9**, Basic fibroblast growth

factor 110590-64-2 127464-60-2, Vascular endothelial growth factor

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(vascularizable biomaterials for creation of three-dimensional tissues)

IT 9002-84-0 9002-88-4, Polyethylene 9002-89-5 9003-01-4, Polyacrylic

acid 9003-05-8, Polyacrylamide 9005-32-7, Alginic acid 9005-38-3D,

Sodium alginate, **RGD** peptide conjugates 25087-26-7,

Polymethacrylic acid 25104-18-1, Polylysine 25322-68-3 34346-01-5,

Lactic acid-glycolic acid copolymer 38000-06-5, Polylysine

99896-85-2D, alginic acid conjugates 156461-57-3, Lactic acid-lysine

copolymer 246867-28-7

RL: BPR (Biological process); BSU (Biological study, unclassified); DEV (Device component use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(vascularizable biomaterials for creation of three-dimensional tissues)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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AN 1999:644000 HCAPLUS

TI Rapid publication Incompatibility between human blood and isolated **islets of langerhans**: a finding with implications for clinical intraportal **islet transplantation**?

AU **Bennet, William**; Sundberg, Berit; Groth, Carl-Gustav; Brendel, Mathias D.; Brandhorst, Daniel; Brandhorst, Heide; Bretzel, Reinhardt G.; Elgue, Graciela; **Larsson, Rolf**; **Nilsson, Bo**; **Korsgren, Olle**

CS Department of Transplantation Surgery Karolinska Institutet, Huddinge Hospital, Huddinge, S-141 86, Swed.

SO Diabetes (1999), 48(10), 1907-1914
CODEN: DIAEAS; ISSN: 0012-1797

PB American Diabetes Association

DT Journal

LA English

AB The remarkable difference in success rates between clin. pancreas **transplantation** and **islet transplantation** is poorly understood. Despite the same histocompatibility barrier and similar immunosuppressive treatments in both **transplantation** procedures, human intraportal **islet transplantation** has a much inferior success rate than does vascularized pancreas **transplantation**. Thus far, little attention has been directed to the possibility that **islets transplanted** into the blood stream may elicit an injurious incompatibility reaction. We have tested this hypothesis in vitro with human **islets** and in vivo with porcine **islets**. Human **islets** were exposed to nonanticoagulated human ABO-compatible blood in surface-heparinized polyvinyl chloride tubing loops. **Heparin** and/or the sol. complement receptor 1 (sCR1) TP10 were tested as additives. Adult porcine **islets** were **transplanted** intraportally into pigs, and the liver was recovered after 60 min for immunohistochem. staining. Human **islets** induced a rapid consumption and activation of platelets. Neutrophils and monocytes were also consumed, and the coagulation and complement systems were activated. Upon histol. examn., **islets** were found to be embedded in clots and infiltrated with CD11+ leukocytes. Furthermore, the cellular morphol. was disrupted. When **heparin** and sCR1 were added to the blood, these events were avoided. Porcine **islets** retrieved in liver biopsies after intraportal **islet allotransplantation** showed a morphol. similar to that of human **islets** perfused in vitro. Thus, exposure of isolated **islets of Langerhans** to allogenic blood resulted in significant damage to the **islets**, a finding that could explain the unsatisfactory clin. results obtained with intraportal **islet transplantation**. Because administration of **heparin** in combination with a sol. complement receptor abrogated these events, such treatment would presumably improve the outcome of clin. **islet transplantation** by reducing both initial **islet** loss and subsequent specific immune responses.

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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- (44) Zimmet, P; J Diabetes Complications 1997, V11, P60 MEDLINE

L65 ANSWER 22 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:451362 HCAPLUS

DN 131:83976

TI Regulated secretion from genetically engineered neuroendocrine cell lines
and its application for gene therapy of diabetes and hypoglycemia

IN Clark, Samuel A.; Thigpen, Anice E.

PA Betagene, Inc., USA

SO PCT Int. Appl., 318 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C12N015-00

CC 3-2 (Biochemical Genetics)

Section cross-reference(s): 1, 2, 63

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 9935255	A2	19990715	WO 1999-US631	19990111 <--
	WO 9935255	A3	19991028		
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, US, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	CA 2318376	AA	19990715	CA 1999-2318376	19990111 <--
	AU 9921131	A1	19990726	AU 1999-21131	19990111 <--
	AU 9924551	A1	19990726	AU 1999-24551	19990111 <--

EP 1045898 A2 20001025 EP 1999-904073 19990111 <--
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO

PRAI US 1998-71193P P 19980112 <--
 US 1998-71209P P 19980112 <--
 US 1998-72556P P 19980112 <--
 US 1998-971209 A2 19980112 <--
 US 1998-87821P P 19980603 <--
 US 1998-87848P P 19980603 <--
 WO 1999-US631 W 19990111 <--
 WO 1999-US633 W 19990111 <--

AB The present invention provides compns. and methods of comprising engineered human neuroendocrine cell lines having a regulated secretory pathway. More particularly, the present invention provides methods and compns. for engineering regulated secretion into cells. Certain aspects of the invention provide glycemic sensing mechanisms to a population of genetically engineered cells. In particular embodiments, the present invention provides compns. and methods of providing indirect glycemic sensing mechanisms to a population of genetically engineered cells. Specifically contemplated are methods and compns. for engineering indirect glucose sensing and glucose counter regulation capacity into cells. Methods of using these cells for minimizing hypoglycemia in diabetic therapy are also disclosed. An engineered cell (.beta.G H03) derived from a human lung carcinoma has potential as an appropriate human cell line for **allotransplantation** and cell-based delivery of **insulin** and other peptide hormones. The .beta.G H03 cell line is sensitive to antibiotics and less susceptible to immunol. destruction than cells **transplanted** across species. Examples of a glucose counter-regulatory system include the following receptor/ligand pairs: .alpha.2-adrenergic receptor/epinephrine or Clonidine; somatostatin receptor/somatostatin or Octreotide; glucocorticoid receptor/glucocorticoids. Each of these receptor/ligand pairs function to inhibit secretion of a polypeptide hormone such as **insulin** from the cell, and can serve to protect patients treated with **transplanted, insulin**-secreting cells from hypoglycemia.

ST neuroendocrine cell secretion genetic engineering; gene therapy diabetes hypoglycemia neuroendocrine implant; **insulin** secretion neuroendocrine cell genetic engineering

IT Transport proteins

RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (GLUT-2 (glucose-transporting, 2); 'regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)

IT Genetic element

RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (IRES (internal ribosomal entry site) element; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)

IT Gastrointestinal hormones

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (PHM; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)

IT Animal cell line

(RIN; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)

IT Glycoproteins, specific or class

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

- (SAP (serum amyloid, P); regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)
- IT Hormones, animal, biological studies
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (amidated; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)
- IT Receptors
 RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (calcium; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)
- IT Intestine
 (cecum; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)
- IT Intestine
 (colon; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)
- IT Polarization
 (depolarization, biol., secretion system regulated with; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)
- IT Gastrointestinal hormone receptors
 Gastrointestinal hormone receptors
 Peptide receptors
 Peptide receptors
 RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (gastric inhibitory polypeptide; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)
- IT Drug delivery systems
 (hydrogels; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)
- IT Transformation, neoplastic
 (immortalization; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)
- IT Drug delivery systems
 (implants; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)
- IT **Pancreatic islet of Langerhans**
 (**insulinoma**; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)
- IT Genetic element
 RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (lexP site; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)
- IT Drug delivery systems
 (liposomes; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)
- IT Encapsulation

- (microencapsulation; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)
- IT Endocrine system
(neuroendocrine system; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)
- IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pancreatic lipase-related; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)
- IT Hormone receptors
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pancreatic polypeptide; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)
- IT Carboxylic acids, biological studies
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phenolic, myco-, selectable marker; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)
- IT Genetic element
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyadenylation signal; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)
- IT Bladder
Diabetes mellitus
Digestive tract
Gene therapy
Hypoglycemia
Liver
Lung
Pancreas
Pancreatic islet of Langerhans
Pituitary gland
Retroviral vectors
Secretion (process)
Stomach
Thyroid gland
Virus vectors
(regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)
- IT Enkephalins
Neurophysins
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)
- IT Glucagon-like peptide-1 receptors
Glucocorticoid receptors
Growth factors, animal
Hepatocyte growth factor
Muscarinic receptors
Platelet-derived growth factors
Promoter (genetic element)

Somatostatin receptors

Sulfonylurea receptors

Vasopressin receptors

RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)

IT Enzymes, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(secreted; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)

IT Dephosphorylation, biological

Phosphorylation, biological

(secretion system regulated with; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)

IT Calmodulins

Fatty acids, biological studies

Glycerides, biological studies

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(secretion system regulated with; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)

IT Antibiotic resistance

(selectable marker; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)

IT Hormone receptors

RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(urocortin; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)

IT Adeno-associated virus

Human adenovirus

Human herpesvirus

Lentivirus

(vector; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)

IT **Pancreatic islet of Langerhans**

(.alpha.-cell; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)

IT Adrenoceptors

RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(.alpha.1; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)

IT Adrenoceptors

RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(.alpha.2; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)

IT Adrenoceptors

Transforming growth factors

RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
 (.beta.-; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)

IT **Pancreatic islet of Langerhans**
 (.beta.-cell; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)

IT Animal cell line
 (.beta.G H03; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)

IT 9005-32-7, ALginic acid
 RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (coating; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)

IT 50-99-7, Glucose, biological studies
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (counter-regulatory system; regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)

IT 50-56-6, Oxytocin, biological studies 113-79-1, Arginine Vasopressin 1393-25-5, Secretin 9001-28-9, Blood-coagulation factor IX 9001-34-7, Galactosidase **9001-62-1**, Lipase 9002-60-2, ACTH, biological studies 9002-61-3, Chorionic gonadotropin 9002-62-4, Prolactin, biological studies 9002-67-9, Luteinizing hormone 9002-68-0, Follicle-stimulating hormone 9002-71-5, Thyroid-stimulating hormone 9002-72-6, Growth hormone **9004-02-8**, Lipoprotein lipase **9004-10-8**, **Insulin**, biological studies 9007-12-9, Calcitonin 9007-92-5, Glucagon, biological studies 9011-97-6, Cholecystokinin 9015-71-8, Corticotropin-releasing hormone 9026-93-1, Adenosine deaminase 9031-14-5, Lecithin:cholesterol acyltransferase 9031-54-3, Sphingomyelinase 9032-75-1, Polygalacturonidase 9033-06-1, Glucosidase 9034-39-3, Growth hormone-releasing factor 9034-40-6, LH-releasing hormone 9034-42-8, .beta.-Melanocyte-stimulating hormone 9034-50-8, Vasotocin 9035-54-5, Placental lactogen 9035-55-6, Lipotropin 9041-90-1, Angiotensin I 9045-90-3, Gastrin I 11128-99-7, Angiotensin II 20988-64-1, Cholecystokinin-(27-33) 24305-27-9, Thyrotropin-releasing hormone 33507-63-0, Substance P 37213-49-3, .alpha.-Melanocyte-stimulating hormone 37221-79-7, Vasoactive intestinal peptide 51110-01-1, Somatostatin **59392-49-3**, Gastric inhibitory peptide 59763-91-6, Pancreatic polypeptide 60254-82-2 60617-12-1, .beta.-Endorphin 80043-53-4, Gastrin-releasing peptide 82785-45-3, Neuropeptide Y 83652-28-2, Calcitonin gene-related peptide 86933-74-6, Neurokinin A 88506-29-0, Adrenorphin 89750-14-1, Glucagon-like peptide I 98824-26-1, .beta.-Calcitonin gene-related peptide 98897-20-2, 5-28-Human Atrial natriuretic factor 106388-42-5, Peptide YY **106602-62-4**, Amylin **107444-51-9**, Human Glucagon-like peptide-1 (7-36 amide) 117148-67-1, Pancreastatin 119418-04-1, Galanin 120298-73-9, Human PTHrP-(1-40) 123626-67-5, Endothelin I 127120-75-6, Galanin message-associated peptide 137348-10-8, Human PTHrP(107-139) 138949-73-2, Human PTHrP-(107-111) 169494-85-3, Leptin 229483-36-7
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (regulated secretion from genetically engineered neuroendocrine cell lines and its application for gene therapy of diabetes and hypoglycemia)

IT 50-23-7, Cortisol 51-41-2, Norepinephrine 51-43-4, Epinephrine 9001-36-9, Glucokinase 11000-17-2, Vasopressin 62031-54-3, Fibroblast

growth factor 62229-50-9, Epidermal growth factor **67763-96-6**,
Insulin-like growth factor 1 127464-60-2, Vascular endothelial
 growth factor

RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)

(regulated secretion from genetically engineered neuroendocrine cell
 lines and its application for gene therapy of diabetes and
 hypoglycemia)

IT 53-57-6, NADPH 56-65-5, 5'-ATP, biological studies 58-64-0, 5'-ADP,
 biological studies 58-68-4, NADH 60-92-4, CAMP 7440-70-2, Calcium,
 biological studies 10102-43-9, Nitric oxide, biological studies
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)

(secretion system regulated with; regulated secretion from genetically
 engineered neuroendocrine cell lines and its application for gene
 therapy of diabetes and hypoglycemia)

IT 53-79-2, Puromycin 1404-04-2, Neomycin 6379-56-2, Hygromycin
 9002-03-3, Dihydrofolate reductase 9002-06-6, Thymidine kinase
 9016-12-0, Guanosine phosphoribosyltransferase 9025-05-2, Cytosine
 deaminase 9028-27-7, Histidinol dehydrogenase 9037-41-6,
 Nitroreductase 11056-06-7, Bleomycin 54576-55-5, Blasticidin S
 deaminase 58798-67-7, Blasticidin 62213-36-9, Neomycin
 phosphotransferase 87110-39-2, Puromycin acetyltransferase 88361-67-5
 181494-14-4, Zeocin

RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)

(selectable marker; regulated secretion from genetically engineered
 neuroendocrine cell lines and its application for gene therapy of
 diabetes and hypoglycemia)

L65 ANSWER 23 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:219716 HCAPLUS

DN 130:234346

TI Compositions and method of stimulating the proliferation and
 differentiation of human fetal and adult pancreatic cells ex vivo

IN Rubin, Jeffrey; Hayek, Alberto; Beattie, Gillian Marguerite; Otonkoski,
 Timo Pyry Juhani; Quaranta, Vito

PA United States Dept. of Health and Human Services, USA; The Whittier
 Institute for Diabetes and Endocrinology

SO U.S., 20 pp., Cont.-in-part of U.S. 5,587,309.

CODEN: USXXAM

DT Patent

LA English

IC ICM A01N001-02

ICS C12N005-08; C07K016-24; A61K038-19

NCL 435366000

CC 9-11 (Biochemical Methods)

Section cross-reference(s): 11, 13, 14, 63

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5888705	A	19990330	US 1997-732230	19970414 <--
	US 5587309	A	19961224	US 1994-235394	19940429 <--
	WO 9529989	A1	19951109	WO 1995-US5521	19950428 <--
	W:			AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG	
	RW:			KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ	
PRAI	US 1994-235394	A2	19940429		<--
	WO 1995-US5521	W	19950428		<--
AB	A method of inducing the proliferation and/or differentiation of human adult pancreatic cells entails contacting primary cultures of such cells with Hepatocyte Growth Factor/Scatter Factor (HGF/SF), thereby inducing a				

proliferation of .beta.-epithelial cells, an increase in the no. of .beta.-epithelial cells which form islet-like cell clusters, and an increase in **insulin** prodn. per cell. The method is improved by culturing the cells on an extracellular matrix such as 804G in the presence of HGF/SF, and is further improved by reaggregating thus-treated cells and contacting said cells with an **insulin** gene upregulating agent such as a poly(ADP-ribose) synthetase inhibitor such as a nicotinamide or benzamide. The method provides increased nos. of functional islet-like cell clusters for **transplantation**.

ST pancreas B cell culture proliferation differentiation **transplant**

IT Extracellular matrix

(804G and BCEM; compns. and method of stimulating the proliferation and differentiation of human fetal and adult pancreatic cells ex vivo)

IT Animal cell line

(804G; compns. and method of stimulating the proliferation and differentiation of human fetal and adult pancreatic cells ex vivo)

IT Animal cell line

(BCEM (bovine corneal endothelium cell); compns. and method of stimulating the proliferation and differentiation of human fetal and adult pancreatic cells ex vivo)

IT Transforming growth factors

RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)

(antibodies to; compns. and method of stimulating the proliferation and differentiation of human fetal and adult pancreatic cells ex vivo)

IT Animal tissue culture

Bioreactors

Cell differentiation

Cell proliferation

Pancreas

Transplant and Transplantation

(compns. and method of stimulating the proliferation and differentiation of human fetal and adult pancreatic cells ex vivo)

IT Hormones, animal, biological studies

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(compns. and method of stimulating the proliferation and differentiation of human fetal and adult pancreatic cells ex vivo)

IT Hepatocyte growth factor

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)

(compns. and method of stimulating the proliferation and differentiation of human fetal and adult pancreatic cells ex vivo)

IT Eye

(cornea, endothelium; compns. and method of stimulating the proliferation and differentiation of human fetal and adult pancreatic cells ex vivo)

IT Gene

(expression; compns. and method of stimulating the proliferation and differentiation of human fetal and adult pancreatic cells ex vivo)

IT Embryo, animal

(fetus; compns. and method of stimulating the proliferation and differentiation of human fetal and adult pancreatic cells ex vivo)

IT Gene, animal

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(for **insulin**; compns. and method of stimulating the proliferation and differentiation of human fetal and adult pancreatic cells ex vivo)

- IT Diabetes mellitus
(**insulin**-dependent; compns. and method of stimulating the proliferation and differentiation of human fetal and adult pancreatic cells ex vivo)
- IT **Transplant and Transplantation**
(**pancreatic islet**; compns. and method of stimulating the proliferation and differentiation of human fetal and adult pancreatic cells ex vivo)
- IT Animal tissue culture
(primary; compns. and method of stimulating the proliferation and differentiation of human fetal and adult pancreatic cells ex vivo)
- IT Antibodies
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(to TGF- β ; compns. and method of stimulating the proliferation and differentiation of human fetal and adult pancreatic cells ex vivo)
- IT **Pancreatic islet of Langerhans**
(**transplant**; compns. and method of stimulating the proliferation and differentiation of human fetal and adult pancreatic cells ex vivo)
- IT **Pancreatic islet of Langerhans**
(**β -cell**; compns. and method of stimulating the proliferation and differentiation of human fetal and adult pancreatic cells ex vivo)
- IT 9061-61-4, Nerve growth hormone **61912-98-9, Insulin**-like growth factor 62229-50-9, Epidermal growth factor **106096-93-9**, Basic fibroblast growth factor 148348-15-6, Fibroblast growth factor 7
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(compns. and method of stimulating the proliferation and differentiation of human fetal and adult pancreatic cells ex vivo)
- IT 55-21-0, Benzamide 98-92-0, Nicotinamide
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(compns. and method of stimulating the proliferation and differentiation of human fetal and adult pancreatic cells ex vivo)
- IT **9004-10-8, Insulin**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(compns. and method of stimulating the proliferation and differentiation of human fetal and adult pancreatic cells ex vivo)
- IT 9055-67-8, Poly(ADP-ribose) synthetase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(inhibitor; compns. and method of stimulating the proliferation and differentiation of human fetal and adult pancreatic cells ex vivo)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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- (2) Otonkoski, T; J Clin Invest 1993, V92, P1459 HCAPLUS
- (3) Quaranta; US 5510263 1996 HCAPLUS
- (4) Rubin; US 5587309 1996 HCAPLUS

L65 ANSWER 24 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:719068 HCAPLUS

DN 129:335819

TI Bioartificial devices and cellular matrixes therefor

IN Usala, Anton-lewis
 PA Encelle Inc, USA
 SO U.S., 34 pp., Cont.-in-part of U.S. Ser. No. 300,429, abandoned.
 CODEN: USXXAM
 DT Patent
 LA English
 IC ICM A61F002-02
 ICS A61K047-30; C12N011-04
 NCL 424424000
 CC 63-7 (Pharmaceuticals)
 Section cross-reference(s): 16
 FAN.CNT 12

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5830492	A	19981103	US 1995-568694	19951207 <--
	CA 2239498	AA	19970612	CA 1996-2239498	19961114 <--
	WO 9720569	A2	19970612	WO 1996-US18209	19961114 <--
	W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9711192	A1	19970627	AU 1997-11192	19961114 <--
	AU 714465	B2	20000106		
	EP 865288	A2	19980923	EP 1996-941993	19961114 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2000507202	T2	20000613	JP 1997-521275	19961114 <--
	ZA 9610297	A	19970618	ZA 1996-10297	19961206 <--
PRAI	US 1992-841973	B2	19920224	<--	
	US 1994-300429	B2	19940902	<--	
	US 1995-568694	A	19951207	<--	
	WO 1996-US18209	W	19961114	<--	
AB	A device for the effective release of cellular moieties, including hormones, wherein a matrix contg. a hormone producing cellular moiety is encapsulated with a non-immunogenic polymeric material of poly-para-xylylene or other arom. based moiety having a membrane portion with a porosity blocking passage of immunogenic agents and permitting passage of effective nutrients for said cellular moiety and the hormone produced thereby, an improved matrix for the storage, manuf., functional testing, and viral infection testing of cellular moieties wherein a collagen based hydrogel is processed to present a liq. phase at host temp. and functions as a substrate for cellular attachment with additives effective for limiting thermal and pressure trauma, and an improved method for the harvesting tissue from organs. A membrane of poly-p-xylylene was mount on a cylindrical sleeve and immersed in water. For an implantable bioartificial pancreatic device, the cellular moiety contains a plurality of insulin -producing islets.				
ST	bioartificial device cellular matrix; pancreatic islet bioartificial device				
IT	Cryopreservation				
	Transplant and Transplantation				
	(bioartificial devices and cellular matrixes)				
IT	Enzymes, biological studies				
	RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)				
	(bioartificial devices and cellular matrixes)				
IT	Transplant and Transplantation				
	(pancreatic islet; bioartificial devices and				

cellular matrixes)

IT **Pancreatic islet of Langerhans**
(**transplant**; bioartificial devices and cellular matrixes)

IT 9001-12-1, Collagenase 9001-92-7, Protease 9002-07-7, Trypsin
9042-14-2, Dextran sulfate 25722-33-2, Poly-p-xylylene 193363-31-4,
Liberase
RL: DEV (Device component use); PEP (Physical, engineering or chemical
process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);
USES (Uses)
(bioartificial devices and cellular matrixes)

IT 52-90-4, Cysteine, biological studies 56-89-3, Cystine, biological
studies 74-79-3D, L-Arginine, analogs, biological studies 79-17-4,
Aminoguanidine 157-06-2, D-Arginine 2149-70-4 9004-54-0, Dextran,
biological studies **9005-49-6, Heparin**, biological
studies 17035-90-4 125978-95-2, Nitric oxide synthase
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
study); USES (Uses)
(bioartificial devices and cellular matrixes)

IT 10102-43-9, Nitric oxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; bioartificial devices and cellular matrixes)

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Anon; WO 9219195 1992 HCAPLUS
(2) Anon; WO 9316685 1993 HCAPLUS
(3) Anon; WO 9519430 1995 HCAPLUS
(4) Lacy; US 5079160 1992
(5) Metrakos, P; Collagen Gel Matrix Promoters Islet Cell Proliferation,
Trnasplantaion Proceeds 1994, V26(6), P3349 HCAPLUS
(6) Metrakos, P; Collagen Gel Matrix Promotes Islet Cell Proliferation 1994
(7) Parisius; US 4797213 1989
(8) Scharp; US 4868121 1989
(9) Scharp; US 5322790 1994

L65 ANSWER 25 OF 49 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:681820 HCAPLUS
DN 130:57152
TI Reversal of hyperglycemia in streptozotocin diabetic mice by
xenotransplantation of microencapsulated rat islets
AU Tatarkiewicz, Krystyna; Sitarek, Elzbieta; Sabat, Marek; Orłowski, Tadeusz
CS Institute of Biocybernetics and Biomedical Engineering, Warsaw, Pol.
SO Annals of Transplantation (1997), 2(2), 20-23
CODEN: ANTRF6; ISSN: 1425-9524
PB PRESSMED
DT Journal
LA English
CC 63-7 (Pharmaceuticals)
Section cross-reference(s): 2, 14

AB Rat pancreatic islets were immunoisolated within alginate capsules with
addnl. polyethyleneimine-protamine-**heparin** highly biocompatible
membrane. Perifusion study in vitro demonstrated satisfactory
similarities between the **insulin** release profiles of
encapsulated and free islets. Concordant **xenotransplantation** of
microencapsulated rat islets significantly prolonged mean time of restored
normoglycemia (46.+-.15 days) in streptozotocin-diabetic BALB/c mice
recipients comparing to uncoated **grafts** (7.+-.2 days).

ST artificial pancreas **xenotransplant** islet alginate microcapsule
coating

IT Pancreas
Pancreas
(artificial; reversal of hyperglycemia in streptozotocin diabetic mice
by **xenotransplantation** of microencapsulated rat islets)

IT Protamines

RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(coating component; reversal of hyperglycemia in streptozotocin diabetic mice by **xenotransplantation** of microencapsulated rat islets)

IT Encapsulation

(microencapsulation; reversal of hyperglycemia in streptozotocin diabetic mice by **xenotransplantation** of microencapsulated rat islets)

IT Transplant and Transplantation

(**pancreatic islet**; reversal of hyperglycemia in streptozotocin diabetic mice by **xenotransplantation** of microencapsulated rat islets)

IT Diabetes mellitus

(reversal of hyperglycemia in streptozotocin diabetic mice by **xenotransplantation** of microencapsulated rat islets)

IT Pancreatic islet of Langerhans

(**transplant**; reversal of hyperglycemia in streptozotocin diabetic mice by **xenotransplantation** of microencapsulated rat islets)

IT Transplant and Transplantation

(**xenotransplant**; reversal of hyperglycemia in streptozotocin diabetic mice by **xenotransplantation** of microencapsulated rat islets)

IT 9002-98-6 9005-49-6, Heparin, biological studies

RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(coating component; reversal of hyperglycemia in streptozotocin diabetic mice by **xenotransplantation** of microencapsulated rat islets)

IT 9005-35-0, Calcium alginate

RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(reversal of hyperglycemia in streptozotocin diabetic mice by **xenotransplantation** of microencapsulated rat islets)

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Ar Rajab, A; Transplantation 1991, V51, P570 HCAPLUS
- (2) Calafiore, R; ASAIO Journal 1992, V38, P34 MEDLINE
- (3) Clayton, H; Transplant Proc 1992, V24, P956 HCAPLUS
- (4) Cole, D; Horm metab Res 1993, V25, P553 HCAPLUS
- (5) Fan, M; Diabetes 1990, V39, P519 MEDLINE
- (6) Fiedor, P; Pancreas 1994, V9, P670 MEDLINE
- (7) Fritschy, W; Diabetologia 1991, V34, P542 HCAPLUS
- (8) Horcher, A; Trans Proc 1994, V26, P784 MEDLINE
- (9) Iwata, H; J Biomed Mat Res 1994, V28, P1201 HCAPLUS
- (10) Kloeck, G; Appl Microbiol Biotechnol 1994, V40, P638 HCAPLUS
- (11) Krestow, M; Transplantation 1991, V51, P651 MEDLINE
- (12) Latif, Z; Transplantation 1988, V45, P827 HCAPLUS
- (13) Lim, F; Science 1980, V210, P908 HCAPLUS
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- (15) Mazaheri, R; Transplantation 1991, V51, P750 MEDLINE
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- (17) Sitarek, E; Bull Pol Ac Sc: Biol Sc 1993, V41, P117
- (18) Soon-Shiong, P; Transplant Proc 1991, V23, P758 MEDLINE
- (19) Sun, A; ASAIO Journal 1992, V38, P125 MEDLINE
- (20) Sun, A; Progress in Artificial Organs 1983, P769
- (21) Tatarkiewicz, K; Artif Organs 1994, V18, P736 HCAPLUS
- (22) Weber, C; Transplant Proc 1991, V23, P764 MEDLINE
- (23) Weber, C; Transplant Proc 1993, V25, P462 MEDLINE

(24) Weber, C; Transplantation 1990, V49, P396 MEDLINE

L65 ANSWER 26 OF 49 HCAPLUS COPYRIGHT 2002 ACS
 AN 1998:144291 HCAPLUS
 DN 128:241404
 TI Comparison of two methods of pancreas islets immunoisolation
 AU Orlowski, T.; Sitarek, E.; Tatarkiewicz, K.; Sabat, M.; Antosiak, M.
 CS Warsaw School of Medicine, Transplantation Institute, Warsaw, Pol.
 SO International Journal of Artificial Organs (1997), 20(12),
 701-703
 CODEN: IJAODS; ISSN: 0391-3988
 PB Wichtig Editore
 DT Journal
 LA English
 CC 9-4 (Biochemical Methods)
 Section cross-reference(s): 14
 AB The efficacy of two methods of **Langerhans islets**
 immunoisolation was compared. For this purpose the function of
islets encapsulated with alginate/polyethylenimin/protamine/
heparin (APPH) or with alginate/poly-L-lysine/alginate (APA)
 membranes was assessed: in vitro according to their survival and response
 to glucose challenges, and in vivo according to their capability to
 provide sufficient **insulin** delivery to maintain normal fasting
 blood glucose following **xenotransplantation** to streptozotocin
 diabetic mice. In vitro **insulin** secretion the response to
 glucose challenge of APPH and APA encapsulated rat **islets**
 reversed the diabetic state of streptozotocin diabetic mice for a longer
 period, than APPH **islet grafts**. This study clearly
 demonstrated the inadequacy of in vitro methods in the prediction of in
 vivo results of **islets transplantation**.
 ST pancreas islet immunoisolation **transplantation**
 microencapsulation
 IT **Pancreatic islet of Langerhans**
Transplant and Transplantation
 (immunoisolation of **pancreas islets** with
 alginate/polyethylenimin/protamine/**heparin** and
 alginate/poly-L-lysine/alginate microencapsulation)
 IT Encapsulation
 (microencapsulation; immunoisolation of pancreas islets with
 alginate/polyethylenimin/protamine/**heparin** and
 alginate/poly-L-lysine/alginate microencapsulation)
 IT Protamines
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (sulfates; immunoisolation of pancreas islets with
 alginate/polyethylenimin/protamine/**heparin** and
 alginate/poly-L-lysine/alginate microencapsulation)
 IT 50-99-7, D-Glucose, biological studies
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
 BIOL (Biological study); OCCU (Occurrence)
 (blood; immunoisolation of pancreas islets with
 alginate/polyethylenimin/protamine/**heparin** and
 alginate/poly-L-lysine/alginate microencapsulation)
 IT 68-04-2, Sodium citrate 103-47-9, CHES 7647-14-5, Sodium chloride,
 biological studies 9002-98-6, Polyethylenimine **9004-10-8**,
Insulin, biological studies 9005-38-3, Sodium alginate
9005-49-6, **Heparin**, biological studies 10043-52-4,
 Calcium chloride (CaCl₂), biological studies 25104-18-1, Poly-L-lysine
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (immunoisolation of pancreas islets with alginate/polyethylenimin/prota
 mine/**heparin** and alginate/poly-L-lysine/alginate
 microencapsulation)

L65 ANSWER 27 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:15958 HCAPLUS
 DN 128:93200
 TI Immobilized organic material with defined active substance release
 IN Wagner, Karl-Heinz; Naarmann, Herbert
 PA Wagner, Karl-Heinz, Germany; Naarmann, Herbert
 SO Ger. Offen., 10 pp.
 CODEN: GWXXBX
 DT Patent
 LA German
 IC ICM C07K017-00
 ICS C07K014-62; C07K014-815; A61K038-58; A61K038-28; A61K031-725
 CC 63-6 (Pharmaceuticals)
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19623440	A1	19971218	DE 1996-19623440	19960612 <--
AB	A bioartificial pancreas for transplantation into human diabetic patients comprises a vascular implant contg. immobilized insulin , proinsulin, preproinsulin, pancreatic islet cells, or APUD cells. The implant preferably contains anticoagulants, antithrombotics, leukocyte adhesion inhibitors, and inhibitors of complement activation and of protein adsorption. Thus, rat pancreatic islet cells were encapsulated in microporous silicone capillary catheters (diam. 500-600 .mu.m; mol. cutoff 50-140 kD) which were implanted in the right cardiac ventricle of a dog. Examn. after 4 wk showed that the encapsulated islet cells received adequate nutrition and oxygenation. Parallel in vitro expts. demonstrated insulin secretion by the encapsulated islet cells, which was stimulated by glucose loading.				
ST	islet cell immobilization artificial pancreas; encapsulation islet cell silicone catheter; vascular implant islet cell immobilization				
IT	Blood (adhesion of components of, inhibition of; immobilized org. material with defined active substance release)				
IT	Blood vessel (artificial; immobilized org. material with defined active substance release)				
IT	Electric potential (biol., controlled release in response to; immobilized org. material with defined active substance release)				
IT	Macromolecular compounds RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (biol.; immobilized org. material with defined active substance release)				
IT	Respiration, animal (by implanted cells; immobilized org. material with defined active substance release)				
IT	Medical goods (catheters; immobilized org. material with defined active substance release)				
IT	Medical goods Medical goods (fabrics; immobilized org. material with defined active substance release)				
IT	Drug delivery systems (films; immobilized org. material with defined active substance release)				
IT	Drug delivery systems (foams; immobilized org. material with defined active substance release)				
IT	Carotid body (glomus cell; immobilized org. material with defined active substance release)				

IT **Anticoagulants**
 Blood vessel
 Immobilization, biochemical
Pancreatic islet of Langerhans
 Polar molecules
 Porous materials
 (immobilized org. material with defined active substance release)

IT Carbon fibers, biological studies
 Macromolecular compounds
 Polymers, biological studies
 RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (immobilized org. material with defined active substance release)

IT Drug delivery systems
 Drug delivery systems
 (implants, controlled-release; immobilized org. material with defined active substance release)

IT Drug delivery systems
 Drug delivery systems
 (microcapsules, controlled-release; immobilized org. material with defined active substance release)

IT Polysiloxanes, biological studies
 RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (microporous, catheters; immobilized org. material with defined active substance release)

IT Porous materials
 (microporous; immobilized org. material with defined active substance release)

IT Adhesion, biological
 (of blood components, inhibition of; immobilized org. material with defined active substance release)

IT Medical goods
 (pads; immobilized org. material with defined active substance release)

IT **Transplant and Transplantation**
 (pancreatic islet; immobilized org. material with defined active substance release)

IT Medical goods
 (sponges; immobilized org. material with defined active substance release)

IT Medical goods
 (tubes; immobilized org. material with defined active substance release)

IT 435-97-2, Marcumar 8001-27-2, Hirudin 9004-10-8, **Insulin**, biological studies 9005-49-6, **Heparin**, biological studies 9035-68-1, Proinsulin 61116-24-3, Preproinsulin
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (immobilized org. material with defined active substance release)

L65 ANSWER 28 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 1997:650432 HCAPLUS

DN 127:231585

TI Storage articles for prolonged viability and function of living cells

IN Soon-Shiong, Patrick; Desai, Neil P.; Moloney, Molly; Yao, Qiang X.

PA Vivorx Pharmaceuticals, Inc., USA; Soon-Shiong, Patrick; Desai, Neil P.;

Moloney, Molly; Yao, Qiang X.

SO PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C12N005-06
ICS C12N011-10; C12N011-04
CC 9-1 (Biochemical Methods)
Section cross-reference(s): 14, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9735958	A1	19971002	WO 1997-US1731	19970130 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9718552	A1	19971017	AU 1997-18552	19970130 <--
PRAI	US 1996-622063		19960326 <--		
	WO 1997-US1731		19970130 <--		
AB	An article has been developed which unexpectedly prolongs the viability of living cells or cell aggregates and which maintains the biol. function and viability of the stored cells for very long periods of time. Also provided is a novel method of storing and culturing cells which is esp. useful for accumulating large nos. of cells for therapeutic purposes, including transplantation into human patients to alleviate disease processes. The invention method involves surrounding cells or cell aggregates with a suitable cell-protective layer, thereby providing articles of various sizes and shapes.				
ST	storage article viability function living cell				
IT	Cell				
	RL: ANT (Analyte); ANST (Analytical study) (Living; storage articles for prolonged viability and function of living cells)				
IT	Blood vessel				
	RL: ANT (Analyte); ANST (Analytical study) (Vassopressor; storage articles for prolonged viability and function of living cells)				
IT	Immunology				
	RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative) (active factor; storage articles for prolonged viability and function of living cells)				
IT	Storage				
	RL: ANT (Analyte); ANST (Analytical study) (articles; storage articles for prolonged viability and function of living cells)				
IT	Endocrine system				
	RL: ANT (Analyte); ANST (Analytical study) (cell; storage articles for prolonged viability and function of living cells)				
IT	Pancreatic islet of Langerhans				
	Thyroid gland				
	RL: ANT (Analyte); ANST (Analytical study) (cells; storage articles for prolonged viability and function of living cells)				
IT	Endocrine system				
	RL: ANT (Analyte); ANST (Analytical study) (chromaffin system, cell; storage articles for prolonged viability and function of living cells)				
IT	Liver				
	(hepatocyte; storage articles for prolonged viability and function of living cells)				
IT	Skin				

RL: ANT (Analyte); ANST (Analytical study)
 (keratinocyte; storage articles for prolonged viability and function of living cells)

IT Nerve
 RL: ANT (Analyte); ANST (Analytical study)
 (neuron; storage articles for prolonged viability and function of living cells)

IT Nucleic acids
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (poly-; storage articles for prolonged viability and function of living cells)

IT Cell
 RL: ANT (Analyte); ANST (Analytical study)
 (stem; storage articles for prolonged viability and function of living cells)

IT **Transplant and Transplantation**
 (storage articles for prolonged viability and function of living cells)

IT Animal tissue culture
Anticoagulants
 Epithelium
 Eukaryote (Eukaryotae)
 Hematopoietic precursor cell
 Immune system
 Muscle
 Neoplasm
 RL: ANT (Analyte); ANST (Analytical study)
 (storage articles for prolonged viability and function of living cells)

IT Blood-coagulation factors
 Cytokines
 Enzymes, biological studies
 Fibrinolytics
 Growth factors, animal
 Hormones, animal, biological studies
 Interferons
 Neurotransmitters
 Opioids
 RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL
 (Biological study); FORM (Formation, nonpreparative)
 (storage articles for prolonged viability and function of living cells)

IT Lipids, biological studies
 Polyamides, biological studies
 Polyesters, biological studies
 Polymers, biological studies
 Polyoxyalkylenes, biological studies
 Polysaccharides, biological studies
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (storage articles for prolonged viability and function of living cells)

IT Interferons
 RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL
 (Biological study); FORM (Formation, nonpreparative)
 (.gamma.; storage articles for prolonged viability and function of living cells)

IT 9003-01-4, Polyacrylic acid
 RL: ANT (Analyte); ANST (Analytical study)
 (storage articles for prolonged viability and function of living cells)

IT 51-41-2, Norepinephrine 51-43-4, Adrenalin 51-61-6, Dopamine,
 biological studies 1407-47-2, Angiotensin 9001-27-8, Factor viii
 9001-28-9, Factor ix 9002-01-1, Streptokinase **9004-10-8,**
Insulin, biological studies **9005-49-6, Heparin**
 , biological studies **9035-68-1**, Proinsulin 9039-53-6,
 Urokinase 9054-89-1, Superoxide dismutase 9061-61-4, Nerve growth

factor 11096-26-7, Erythropoietin 51110-01-1, Somatostatin
62683-29-8, Colony stimulating factor 139639-23-9, Tissue plasminogen
activator

RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL
(Biological study); FORM (Formation, nonpreparative)

(storage articles for prolonged viability and function of living cells)

IT 9002-89-5, Polyvinyl alcohol 9003-05-8, Polyacrylamide 9003-39-8,
Polyvinyl pyrrolidinone 9005-32-7D, Alginic acid, polymer 56688-68-7,
.alpha.-L-Guluronic acid

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)

(storage articles for prolonged viability and function of living cells)

L65 ANSWER 29 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 1997:450109 HCAPLUS

DN 127:60628

TI Combination therapeutic methods employing nitric oxide scavengers

IN Lai, Ching-San

PA Medinox, Inc., USA; Lai, Ching-San

SO PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-325

CC 1-12 (Pharmacology)

Section cross-reference(s): 63

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9718805	A1	19970529	WO 1996-US18124	19961112 <--
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	US 5747532	A	19980505	US 1995-561594	19951121 <--
	CA 2238028	AA	19970529	CA 1996-2238028	19961112 <--
	AU 9676784	A1	19970611	AU 1996-76784	19961112 <--
	EP 866695	A1	19980930	EP 1996-939670	19961112 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
	CN 1202824	A	19981223	CN 1996-198435	19961112 <--
	JP 2000500493	T2	20000118	JP 1997-519776	19961112 <--
	AU 9869984	A1	19980730	AU 1998-69984	19980609 <--
	AU 722361	B2	20000803		
PRAI	US 1995-561594	A2	19951121 <--		
	US 1996-12820P	P	19960305 <--		
	WO 1996-US18124	W	19961112 <--		

OS MARPAT 127:60628

AB Combination therapeutic methods are provided for the in vivo inactivation or inhibition of formation (either directly or indirectly) of species which induce the expression of nitric oxide synthase, as well as reducing nitric oxide levels produced as a result of NO synthase expression. In contrast to the inhibitory approach described in the prior art (i.e., wherein the function of the enzymes responsible for nitric oxide prodn. is inhibited), the present invention employs a combination of inactivation (or inhibition) and scavenging approaches, whereby the stimulus of nitric oxide synthase expression is inactivated, or the prodn. thereof is inhibited, and overproduced nitric oxide is bound in vivo to a suitable nitric oxide scavenger. The resulting complexes render the stimulus of

nitric oxide synthase expression inactive (or inhibit the prodn. thereof), and nitric oxide harmless. The resulting complexes are eventually excreted in the urine of the host. Also provided are compns. and formulations useful for carrying out the above methods.

- ST NO synthase inhibitor combination therapeutic; nitric oxide scavenger combination therapeutic
- IT Proteins, specific or class
 - RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (BPI (bactericidal/permeability-increasing); nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Intestine, disease
 - (Crohn's, therapeutic agents for; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Complement
 - (activation, inhibitors; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT **Transplant and Transplantation**
 - Transplant and Transplantation**
 - (allotransplant, heart; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Heart
 - Heart
 - (allotransplant; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Interleukin 1 receptors
 - Platelet-activating factor receptors
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (antagonists; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Interleukin 6
 - Tumor necrosis factors
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (antibodies to; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Tear (ocular fluid)
 - (artificial; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Ion channel blockers
 - Ion channel blockers
 - (calcium, dihydropyridine; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Drug delivery systems
 - (drops; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Drug delivery systems
 - (emulsions; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Toxins
 - RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 - (endotoxins; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Drug delivery systems
 - (inhalants; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Drug delivery systems
 - (injections, i.v.; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Drug delivery systems
 - (injections, s.c.; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)

- IT Proteins, specific or class
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (iron-contg.; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Proteins, specific or class
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (lipopolysaccharide-binding, sol.; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Drug delivery systems
 (liposomes; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Drug delivery systems
 (liqs., dispersions; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Antibodies
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (monoclonal, OKT3; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Anti-inflammatory agents
Anticoagulants
 Antidiabetic agents
 Antihypotensives
 Bacteria (Eubacteria)
 Drug delivery systems
 Drugs
 Immunosuppressants
Pancreatic islet of Langerhans
 Scavengers
Transplant rejection
 (nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Antibiotics
 Antibodies
 Corticosteroids, biological studies
 Interleukin 10
 Interleukin 13
 Interleukin 4
 Metalloporphyrins
 Porphyrins
 Prostaglandins
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Blood-coagulation factors
 Bradykinin receptors
 Cytokine receptors
 Cytokines
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Leukotriene antagonists
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(non-heme iron-contg.; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)

IT Drug delivery systems
(ophthalmic; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)

IT Drug delivery systems
(oral; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)

IT Drug delivery systems
(parenterals; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)

IT Drug delivery systems
(rectal; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)

IT Shock (circulatory collapse)
(septic; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)

IT CD14 (antigen)
Tumor necrosis factor receptors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sol.; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)

IT Drug delivery systems
(solids; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)

IT Drug delivery systems
(solns.; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)

IT Eye, disease
(therapeutic agents for; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)

IT Globulins, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thymoglobulin; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)

IT Complement receptors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type 1, sol.; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)

IT Transition metal complexes
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(with dithiocarbamates; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)

IT Transforming growth factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.-; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)

IT Interferons
RL: BSU (Biological study, unclassified); BIOL (Biological study)

- (.gamma., antibodies to; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT Interferon receptors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.gamma.-interferon, sol.; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT 9001-30-3, Blood coagulation factor XII 80295-54-1, Complement C5a
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibodies to; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT 9025-82-5, Phosphodiesterase 9029-60-1, Lipoxygenase 39391-18-9, Cyclooxygenase 57576-52-0, Thromboxane A2 80295-70-1, C1 Esterase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT 506-32-1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metabolites; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT 140608-64-6, Muromonab CD3
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT 50-02-2 50-24-8, Prednisolone 50-33-9, Phenylbutazone, biological studies 50-44-2, 6-Mercaptopurine 50-78-2, Aspirin 53-86-1, Indomethacin 59-66-5, Acetazolamide 70-51-9, Desferrioxamine 79-17-4, Aminoguanidine 83-43-2, Methylprednisolone 89-57-6, Mesalamine 92-13-7, Pilocarpine 443-48-1, Metronidazole 446-86-6, Azathioprine 512-15-2, Cyclopentolate 594-07-0D, Dithiocarbamic acid, dithiocarbamates 599-79-1, Sulfasalazine 737-86-0, Pyridoxal isonicotinoyl hydrazone 867-44-7 1404-26-8, Polymyxin B 2418-14-6, Dimercaptosuccinic acid 4428-95-9, Foscarnet 7439-89-6D, Iron, dithiocarbamate complexes, biological studies 7439-96-5D, Manganese, dithiocarbamate complexes, biological studies 7440-48-4D, Cobalt, dithiocarbamate complexes, biological studies 7440-50-8D, Copper, dithiocarbamate complexes, biological studies 9004-10-8, Insulin, biological studies 12678-01-2, Phenanthroline 22664-55-7, Metipranolol 24280-93-1, Mycophenolic acid 24584-09-6, ICRF-187 26839-75-8, Timolol 30652-11-0, 1,2-Dimethyl-3-hydroxypyrid-4-one 47141-42-4, Levobunolol 53774-63-3 53882-12-5, Lodoxamide 73384-59-5, Ceftriaxone 79217-60-0, Cyclosporin 82410-32-0, Ganciclovir 94161-07-6, N-Methyl-D-glucamine dithiocarbamate 94161-07-6D, N-Methyl-D-glucamine dithiocarbamate, iron complexes 104987-11-3, FK506 106602-62-4, Amylin 160525-37-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT 58-82-2, Bradykinin 10102-43-9, Nitric oxide, biological studies 65154-06-5, Platelet-activating factor 125978-95-2, Nitric oxide synthase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)
- IT 69-72-7, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(salicylates; nitric oxide-scavenging and nitric oxide synthase-inhibiting combinations for therapeutic use)

L65 ANSWER 30 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 1997:205254 HCAPLUS

DN 126:198546

TI Autologous immune cell therapy: cell compositions, methods and applications to treatment of human disease

IN Gruenberg, Michael L.

PA Celltherapy, Inc., USA; Gruenberg, Michael L.

SO PCT Int. Appl., 98 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C12N005-08

ICS A61K035-14

CC 15-1 (Immunochemistry)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9705239	A1	19970213	WO 1996-US12170	19960725	<--
	W:					AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE
	RW:					KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM
	CA 2227327	AA	19970213	CA 1996-2227327	19960724	<--
	JP 2001520509	T2	20011030	JP 1997-507706	19960724	<--
	AU 9666499	A1	19970226	AU 1996-66499	19960725	<--
	EP 852618	A1	19980715	EP 1996-926117	19960725	<--
	R:					AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI
	US 2002182730	A1	20021205	US 1998-127411	19980731	<--
	US 2001031253	A1	20011018	US 2001-824906	20010402	<--
PRAI	US 1995-506668	A	19950725			<--
	US 1995-44693P	P	19950726			<--
	US 1996-700565	A3	19960725			<--
	WO 1996-US12170	W	19960725			<--
AB	Compns. contg. substantially homogeneous populations of functionally or phenotypically defined immune cells that have been isolated from a patient and expanded and/or differentiated ex vivo. The immune cells are effector or memory or regulatory T cells, Th1 cells, Th2 cells, Th3 cells, CD4+ cells, CD8+ cells, etc. The cell population expansion is activated by sp. surface protein, interferon-.gamma., interleukin 2, interleukin 4, anti-.gamma. interferon, anti-interleukin 12, monoclonal antibody to CD3, CD2, CD4, CD8, CD11a, CD27, CD28, CD44, or CD45RO, and is performed in a hollow fiber bioreactor. Methods for treating or preventing disease or otherwise altering the immune status of the patient by reinfusing such cells into the donor are also provided. The autologous immune cell therapy is used for treating autoimmune disease, chronic inflammation, allergy, infection, organ or tissue transplant rejection, rheumatoid arthritis, inflammatory bowel disease, insulin -dependent diabetes mellitus, tumor, multiple sclerosis, Crohn's disease, HIV infection, etc.					
ST	autologous immune cell therapy autoimmune disease					
IT	CD antigens					
	RL: BSU (Biological study, unclassified); BIOL (Biological study)					
	(CD27; autologous immune cell therapy for treatment of human diseases)					
IT	Intestine, disease					
	(Crohn's; autologous immune cell therapy for treatment of human diseases)					
IT	Glycoproteins, specific or class					

- RL: BSU (Biological study, unclassified); BIOL (Biological study)
(H-CAM (homing cell adhesion mol.); autologous immune cell therapy for treatment of human diseases)
- IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(alloantigens; autologous immune cell therapy for treatment of human diseases)
- IT **Transplant and Transplantation**
(**allotransplant**, organ; autologous immune cell therapy for treatment of human diseases)
- IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antigens CD11a; autologous immune cell therapy for treatment of human diseases)
- IT Allergy
Animal tissue
Autoimmune disease
Body fluid
CD4-positive T cell
CD8-positive T cell
Cell differentiation
Human immunodeficiency virus
Human immunodeficiency virus 1
Immunosuppressants
Infection
Mononuclear cell (leukocyte)
Neoplasm
Pathogen
Rheumatoid arthritis
Transplant rejection
Vaccines
(autologous immune cell therapy for treatment of human diseases)
- IT Antibodies
Antigens
Interleukin 2
Interleukin 4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(autologous immune cell therapy for treatment of human diseases)
- IT **Integrins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(autologous immune cell therapy for treatment of human diseases)
- IT CD2 (antigen)
CD28 (antigen)
CD3 (antigen)
CD4 (antigen)
CD44 (antigen)
CD45RO (antigen)
CD8 (antigen)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(autologous immune cell therapy for treatment of human diseases)
- IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cell surface; autologous immune cell therapy for treatment of human diseases)
- IT Inflammation
(chronic; autologous immune cell therapy for treatment of human diseases)
- IT T cell (lymphocyte)

- (cytotoxic; autologous immune cell therapy for treatment of human diseases)
- IT Lymphocyte
(effector cell; autologous immune cell therapy for treatment of human diseases)
- IT Myelin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(encephalitogenic epitope; autologous immune cell therapy for treatment of human diseases)
- IT T cell (lymphocyte)
(helper cell, Th3; autologous immune cell therapy for treatment of human diseases)
- IT T cell (lymphocyte)
(helper cell/inducer, TH1; autologous immune cell therapy for treatment of human diseases)
- IT T cell (lymphocyte)
(helper cell/inducer, TH2; autologous immune cell therapy for treatment of human diseases)
- IT Fibers
RL: DEV (Device component use); USES (Uses)
(hollow bioreactor; autologous immune cell therapy for treatment of human diseases)
- IT Bioreactors
(hollow-fiber membrane; autologous immune cell therapy for treatment of human diseases)
- IT Intestine, disease
(inflammatory; autologous immune cell therapy for treatment of human diseases)
- IT Drug delivery systems
(infusions; autologous immune cell therapy for treatment of human diseases)
- IT Diabetes mellitus
(**insulin**-dependent; autologous immune cell therapy for treatment of human diseases)
- IT CD antigens
CD antigens
Integrins
Integrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**integrin** .beta.7; autologous immune cell therapy for treatment of human diseases)
- IT T cell (lymphocyte)
(memory; autologous immune cell therapy for treatment of human diseases)
- IT **Antibodies**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**monoclonal**; autologous immune cell therapy for treatment of human diseases)
- IT **Transplant and Transplantation**
(**pancreatic islet**; autologous immune cell therapy for treatment of human diseases)
- IT Cytokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prodn. profile; autologous immune cell therapy for treatment of human diseases)
- IT T cell (lymphocyte)
(regulatory and effector; autologous immune cell therapy for treatment of human diseases)
- IT Immunological accessory cell
(regulatory; autologous immune cell therapy for treatment of human diseases)

diseases)
 IT **Transplant and Transplantation**
 (tissue; autologous immune cell therapy for treatment of human diseases)
 IT **Pancreatic islet of Langerhans**
 (**transplant**; autologous immune cell therapy for treatment of human diseases)
 IT Intestine, disease
 (ulcerative colitis; autologous immune cell therapy for treatment of human diseases)
 IT **Transplant and Transplantation**
 (**xenotransplant**, organ; autologous immune cell therapy for treatment of human diseases)
 IT **Integrins**
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (.alpha.4; autologous immune cell therapy for treatment of human diseases)
 IT Interferons
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (.gamma.; autologous immune cell therapy for treatment of human diseases)

L65 ANSWER 31 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 1997:27039 HCAPLUS

DN 126:72334

TI Method of stimulating proliferation and differentiation of human fetal pancreatic cells ex vivo

IN Rubin, Jeffrey; Hayek, Alberto; Beattie, Gillian M.; Otonkoski, Timo P. J.

PA United States Dept. of Health and Human Services, USA; Whittler Institute for Diabetes and Endocrinology

SO U.S., 9 pp.

CODEN: USXXAM

DT Patent

LA English

IC ICM C12N005-00

ICS C12N005-02

NCL 435240200

CC 9-11 (Biochemical Methods)

Section cross-reference(s): 14, 63

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5587309	A	19961224	US 1994-235394	19940429 <--
	CA 2189052	AA	19951109	CA 1995-2189052	19950428 <--
	WO 9529989	A1	19951109	WO 1995-US5521	19950428 <--
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ				
	AU 9524336	A1	19951129	AU 1995-24336	19950428 <--
	AU 695390	B2	19980813		
	EP 765385	A1	19970402	EP 1995-918374	19950428 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 10503923	T2	19980414	JP 1995-528510	19950428 <--
	US 5888705	A	19990330	US 1997-732230	19970414 <--
PRAI	US 1994-235394	A	19940429	<--	
	WO 1995-US5521	W	19950428	<--	
AB	A method of inducing the proliferation and/or differentiation of human fetal pancreatic cells entails contacting such cells in primary culture with hepatocyte growth factor/scatter factor, thereby inducing a				

proliferation of .beta.-epithelial cells, an increase in the no. of .beta.-epithelial cells which form islet-like cell clusters, and an increase in **insulin** prodn. per cell. The method provides increased nos. of functional islet-like cell clusters for **transplantation**, for example, into Type 1 diabetic patients. The method can be scaled up to provide clin. useful nos. of cells for **transplantation**.

- ST pancreatic islet cell culture **transplantation** diabetes;
hepatocyte growth factor pancreas cell culture; fetus pancreas cell culture **transplantation** diabetes; beta cell pancreatic islet proliferation culture; **insulin** producing islet cell culture **transplantation**
- IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(anti-TGF-.beta.; human fetal pancreatic cell culture for **transplantation** in diabetes)
- IT Embryo, animal
(fetus; human fetal pancreatic cell culture for **transplantation** in diabetes)
- IT Bioreactors
Cell differentiation
Cell proliferation
Pancreas
 Pancreatic islet of Langerhans
Therapy
 Transplant and Transplantation
 (human fetal pancreatic cell culture for **transplantation** in diabetes)
- IT Hepatocyte growth factor
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(human fetal pancreatic cell culture for **transplantation** in diabetes)
- IT Drug delivery systems
(infusions; human fetal pancreatic cell culture for **transplantation** in diabetes)
- IT Diabetes mellitus
(**insulin**-dependent; human fetal pancreatic cell culture for **transplantation** in diabetes)
- IT **Transplant and Transplantation**
(**pancreas**; human fetal pancreatic cell culture for **transplantation** in diabetes)
- IT **Transplant and Transplantation**
(**pancreatic islet**; human fetal pancreatic cell culture for **transplantation** in diabetes)
- IT Animal tissue culture
(primary; human fetal pancreatic cell culture for **transplantation** in diabetes)
- IT Pancreas
 Pancreatic islet of Langerhans
 (**transplant**; human fetal pancreatic cell culture for **transplantation** in diabetes)
- IT Transforming growth factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(.beta.-; human fetal pancreatic cell culture for **transplantation** in diabetes)
- IT **Pancreatic islet of Langerhans**
(.beta.-cell; human fetal pancreatic cell culture for **transplantation** in diabetes)

IT 67763-96-6, IGF-I 67763-97-7, IGF-II 106096-93-9
 , FGF-2 148348-15-6, FGF-7
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (human fetal pancreatic cell culture for **transplantation** in diabetes)
 IT 9004-10-8, **Insulin**, biological studies
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
 (human fetal pancreatic cell culture for **transplantation** in diabetes)

L65 ANSWER 32 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 1996:380155 HCAPLUS

DN 125:31943

TI Binding agents to CD23

IN Bonnefoy, Jean-Yves Marcel Paul

PA Glaxo Group Limited, UK

SO PCT Int. Appl., 50 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07K016-28

ICS A61K039-395

CC 15-3 (Immunochemistry)

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9612741	A1	19960502	WO 1995-EP4109	19951020	<--
	W:	AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ				
	RW:	KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2203363	AA	19960502	CA 1995-2203363	19951020	<--
	CA 2203364	AA	19960502	CA 1995-2203364	19951020	<--
	AU 9538435	A1	19960515	AU 1995-38435	19951020	<--
	AU 698158	B2	19981022			
	EP 788513	A1	19970813	EP 1995-936525	19951020	<--
	EP 788513	B1	20010124			
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09511757	T2	19971125	JP 1995-513508	19951020	<--
	BR 9509498	A	19971223	BR 1995-9498	19951020	<--
	CN 1169735	A	19980107	CN 1995-196799	19951020	<--
	CN 1171119	A	19980121	CN 1995-197075	19951020	<--
	HU 77572	A2	19980629	HU 1998-339	19951020	<--
	EP 1018517	A2	20000712	EP 1999-204301	19951020	<--
	EP 1018517	A3	20000726			
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
	AT 198895	E	20010215	AT 1995-936525	19951020	<--
	ES 2154741	T3	20010416	ES 1995-936525	19951020	<--
	JP 2001316291	A2	20011113	JP 2001-127383	19951020	<--
	JP 3323508	B2	20020909	JP 1996-513508	19951020	<--
	ZA 9508947	A	19960731	ZA 1995-8947	19951023	<--
	IL 115733	A1	19991222	IL 1995-115733	19951024	<--
	FI 9701756	A	19970424	FI 1997-1756	19970424	<--
	NO 9701902	A	19970424	NO 1997-1902	19970424	<--
PRAI	GB 1994-21463	A	19941025			<--

GB 1995-12480 A 19950620 <--
 GB 1995-13415 A 19950630 <--
 EP 1995-936525 A3 19951020 <--
 JP 1996-513508 A3 19951020 <--
 WO 1995-EP4109 W 19951020 <--

AB Binding agents to CD23 useful in the treatment of inflammatory, autoimmune or allergic diseases. The binding agent is a humanized **antibody** or fragment. Demonstrated in examples were preventative treatment of mice against arthritis using **monoclonal anti-CD23 antibody**, CD23-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c **monoclonal antibodies** decrease CD23-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant CD23 to CD11b and CD11c, etc.

ST humanized chimeric antibody fragment CD23 inflammation; allergy autoimmune disease CD23 antibody fragment

IT Allergy
 Arthritis
 Asthma
 Autoimmune disease
 Dermatitis
 Diabetes mellitus
 Eczema
 Inflammation
 Lupus erythematosus
 Multiple sclerosis
 Psoriasis
 Sjogren's syndrome
 Urticaria
 (humanized and/or chimeric antibody or fragment specific for CD23 for treating inflammatory, autoimmune or allergic diseases)

IT Antibodies
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (humanized and/or chimeric antibody or fragment specific for CD23 for treating inflammatory, autoimmune or allergic diseases)

IT Intestine, disease
 (Crohn's, humanized and/or chimeric antibody or fragment specific for CD23 for treating inflammatory, autoimmune or allergic diseases)

IT **Immunoglobulin receptors**
Receptors
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (Fc.epsilon.RII (IgE fragment Fc receptor II), humanized and/or chimeric antibody or fragment specific for CD23 for treating inflammatory, autoimmune or allergic diseases)

IT Lung, disease
 (chronic obstructive, humanized and/or chimeric antibody or fragment specific for CD23 for treating inflammatory, autoimmune or allergic diseases)

IT **Pancreatic islet of Langerhans**
 (disease, insulinitis, humanized and/or chimeric antibody or fragment specific for CD23 for treating inflammatory, autoimmune or allergic diseases)

IT Nose
 (disease, rhinitis, humanized and/or chimeric antibody or fragment specific for CD23 for treating inflammatory, autoimmune or allergic diseases)

IT Bronchi
 (diseases, bronchitis, humanized and/or chimeric antibody or fragment specific for CD23 for treating inflammatory, autoimmune or allergic diseases)

- IT Kidney, disease
(glomerulonephritis, humanized and/or chimeric antibody or fragment specific for CD23 for treating inflammatory, autoimmune or allergic diseases)
- IT **Transplant and Transplantation**
(**graft-vs.-host reaction**, humanized and/or chimeric antibody or fragment specific for CD23 for treating inflammatory, autoimmune or allergic diseases)
- IT Intestine, disease
(inflammatory, humanized and/or chimeric antibody or fragment specific for CD23 for treating inflammatory, autoimmune or allergic diseases)
- IT **Antibodies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**monoclonal**, humanized and/or chimeric **antibody** or fragment specific for CD23 for treating inflammatory, autoimmune or allergic diseases)
- IT Kidney, disease
(nephrotic syndrome, humanized and/or chimeric antibody or fragment specific for CD23 for treating inflammatory, autoimmune or allergic diseases)
- IT Arthritis
(rheumatoid, humanized and/or chimeric antibody or fragment specific for CD23 for treating inflammatory, autoimmune or allergic diseases)
- IT Thyroid gland, disease
(thyroiditis, Mashimotos; humanized and/or chimeric antibody or fragment specific for CD23 for treating inflammatory, autoimmune or allergic diseases)
- IT Intestine, disease
(ulcerative colitis, humanized and/or chimeric antibody or fragment specific for CD23 for treating inflammatory, autoimmune or allergic diseases)
- IT Eye, disease
(uveitis, humanized and/or chimeric antibody or fragment specific for CD23 for treating inflammatory, autoimmune or allergic diseases)

L65 ANSWER 33 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 1996:380154 HCAPLUS

DN 125:56235

TI Binding agents for treatment of inflammatory, autoimmune or allergic diseases

IN Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille

PA Glaxo Group Limited, UK

SO PCT Int. Appl., 51 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07K016-28

ICS C07K016-46; C07K014-05; C07K014-745; A61K039-395

CC 15-3 (Immunochemistry)

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9612742	A1	19960502	WO 1995-EP4110	19951020 <--
	W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2203363	AA	19960502	CA 1995-2203363	19951020 <--
	CA 2203364	AA	19960502	CA 1995-2203364	19951020 <--
	AU 9538679	A1	19960515	AU 1995-38679	19951020 <--

AU 710369	B2	19990916		
EP 788514	A1	19970813	EP 1995-937803	19951020 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
BR 9509434	A	19980106	BR 1995-9434	19951020 <--
CN 1169735	A	19980107	CN 1995-196799	19951020 <--
CN 1171119	A	19980121	CN 1995-197075	19951020 <--
HU 77572	A2	19980629	HU 1998-339	19951020 <--
JP 10507460	T2	19980721	JP 1995-513642	19951020 <--
EP 1018517	A2	20000712	EP 1999-204301	19951020 <--
EP 1018517	A3	20000726		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
ES 2154741	T3	20010416	ES 1995-936525	19951020 <--
JP 2001316291	A2	20011113	JP 2001-127383	19951020 <--
ZA 9508947	A	19960731	ZA 1995-8947	19951023 <--
IL 115733	A1	19991222	IL 1995-115733	19951024 <--
PRAI GB 1994-21463	A	19941025	<--	
GB 1995-12480	A	19950620	<--	
GB 1995-13415	A	19950630	<--	
EP 1995-936525	A3	19951020	<--	
JP 1996-513508	A3	19951020	<--	
WO 1995-EP4110	W	19951020	<--	
AB	Binding agents to CD11b, CD11c, CD21, CD23, a 70 to 85 KDa protein expressed on endothelial cells or a 115 KDa protein expressed on endothelial cells, can be useful in the treatment of inflammatory, autoimmune or allergic disease. The binding agent is a humanized antibody or fragment. Demonstrated in examples were CD23-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal antibodies decrease CD23-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant CD23 to CD11b and CD11c, competition of CD23-liposomes with Epstein-Barr virus, interferon .alpha., C3 peptide and C3d,g, etc.			
ST	humanized chimeric antibody fragment CD11b CD11c; CD23 CD21 antibody inflammation autoimmune disease; allergy antibody fragment CD11b CD11c CD21			
IT	Proteins RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (70,000~85,000 mol. wt.; humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)			
IT	Human herpesvirus 4 RL: BIOL (Biological study); USES (Uses) (factor X; humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)			
IT	Glycoproteins RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (gp350/220; Epstein-Barr virus; humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)			
IT	Allergy Arthritis Asthma Autoimmune disease Dermatitis Diabetes mellitus Eczema Inflammation Lupus erythematosus Multiple sclerosis			

Psoriasis

Rheumatoid arthritis

Sjogren's syndrome

Urticaria

(humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)

IT Antibodies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)

IT Proteins

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(115,000-mol.-wt., humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)

IT Intestine, disease

(Crohn's, humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)

IT **Immunoglobulin receptors**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(IgE type II, humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)

IT **Integrins**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(antigens CD11b, humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)

IT **Integrins**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(antigens CD11c, humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)

IT Bronchi

(bronchitis, humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)

IT Lung, disease

(chronic obstructive, humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)

IT Kidney, disease

(glomerulonephritis, humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)

IT **Transplant and Transplantation**

(**graft-vs.-host reaction**, humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)

IT Intestine, disease

(inflammatory, humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)

IT **Pancreatic islet of Langerhans**

(**insulinitis**, humanized or chimeric antibody and fragments as

- binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)
- IT Kidney, disease
(nephrotic syndrome, humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)
- IT Nose
(rhinitis, humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)
- IT Thyroid gland, disease
(thyroiditis, Hashimoto's; humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)
- IT Complement receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(type 2, humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)
- IT Intestine, disease
(ulcerative colitis, humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)
- IT Eye, disease
(uveitis, humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)
- IT Interferons
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.alpha., humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)
- IT 9001-29-0, Blood-coagulation factor X
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Epstein-Barr virus; humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)
- IT 80295-41-6, Complement C3 82903-93-3, Complement C3dg
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)
- IT 177994-56-8
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(humanized or chimeric antibody and fragments as binding agent to CD11b, CD21, CD11c, for treating inflammatory, autoimmune or allergic diseases)

L65 ANSWER 34 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 1996:305579 HCAPLUS

DN 125:8340

TI Role of adhesion molecules in islet allo- and **xenograft** rejection

AU Gotoh, M.; Ohzato, H.; Fukuzaki, T.; Ohta, Y.; Nishihara, M.; Hasuike, M.; Umeshita, K.; Sakon, M.; Yagita, H.; et al.

CS Medical School, Osaka University, Suita, 565, Japan

SO Transplantation Proceedings (1996), 28(2), 617

CODEN: TRPPA8; ISSN: 0041-1345

PB Appleton & Lange

DT Journal

LA English
 CC 15-10 (Immunochemistry)
 AB The authors examd. the roles of LFA-1 and ICAM-1 mols. in islet allo- and **xenograft** rejection using species-specific **monoclonal antibodies**.
 ST adhesion mol islet **graft** rejection
 IT Glycoproteins, specific or class
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (ICAM-1 (intercellular adhesion mol. 1), adhesion mols. role in pancreatic islet allo- and **xenograft** rejection)
 IT **Transplant and Transplantation**
 (allo-, adhesion mols. role in **pancreatic islet** allo- and **xenograft** rejection)
 IT **Pancreatic islet of Langerhans**
 (allotransplant, adhesion mols. role in pancreatic islet allo- and **xenograft** rejection)
 IT **Integrins**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (antigens LFA-1, adhesion mols. role in pancreatic islet allo- and **xenograft** rejection)
 IT **Transplant and Transplantation**
 (**xeno**-, adhesion mols. role in **pancreatic islet** allo- and **xenograft** rejection)
 IT **Pancreatic islet of Langerhans**
 (**xenotransplant**, adhesion mols. role in pancreatic islet allo- and **xenograft** rejection)

L65 ANSWER 35 OF 49 HCAPLUS COPYRIGHT 2002 ACS
 AN 1996:142192 HCAPLUS
 DN 124:173443
 TI Methods for inhibiting antigen specific T cell responses
 IN Blazar, Bruce R.; Vallera, Daniel A.
 PA Regents of the University of Minnesota, USA
 SO PCT Int. Appl., 61 pp.
 CODEN: PIXXD2

DT Patent
 LA English
 IC ICM A61K039-00
 ICS C07K014-705; C07K014-725; C07K016-28; C07K019-00
 CC 15-3 (Immunochemistry)
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9534320	A2	19951221	WO 1995-US7351	19950607 <--
	WO 9534320	A3	19960118		
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2191733	AA	19951221	CA 1995-2191733	19950607 <--
	AU 9527018	A1	19960105	AU 1995-27018	19950607 <--
	EP 784482	A2	19970723	EP 1995-922279	19950607 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 10501815	T2	19980217	JP 1995-502351	19950607 <--
	AU 9947458	A1	19991028	AU 1999-47458	19990908 <--
	AU 748561	B2	20020606		
PRAI	US 1994-255267	A	19940607	<--	
	US 1995-472697	A	19950606	<--	
	AU 1995-27018	A3	19950607	<--	
	WO 1995-US7351	W	19950607	<--	
AB	Methods for inhibiting antigen-specific T cell responses by use of an agent which inhibits a costimulatory signal in T cells are disclosed. Preferably, both a first agent which inhibits a costimulatory signal in the T cell and a second agent which inhibits adhesion of the T cell to a cell presenting antigen to the T cell, are used to inhibit				

antigen-specific T cell responses. For example, anti-LFA-1 antibody, that inhibits adhesion of a T cell to a cell presenting antigen, can be used in conjunction with a CTLA4-Ig fusion protein which inhibits a costimulatory signal in the T cell. Alternatively, another agent which inhibits a costimulatory signal in T cells, such as an anti-B7-1 antibody or an anti-B7-2 antibody can be used with a second agent which inhibits a proliferative signal in the T cell e.g., an anti-IL-2 receptor antibody. The methods of the invention are particularly useful for inhibiting **graft** vs. host disease and for inhibiting rejection of a **transplanted** tissue or organ.

ST T cell signal adhesion receptor inhibitor; **monoclonal antibody** adhesion mol lymphokine receptor; **graft** versus host disease organ **transplant**

IT Antigens

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(CD48; **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Antigens

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(CD49; **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Antigens

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(CD61P; **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Animal growth regulators

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(T cell growth factor; **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Bone marrow

(cell; **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Immunoglobulins

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fusion protein; **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Hematopoietic precursor cell

(**monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Antigens

RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant**

- recipients)
- IT Receptors
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(**monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT **Antibodies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT Blood corpuscle
(peripheral; **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT Animal tissue
(**transplant**; **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT Antigens
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(B 7.2, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT Antigens
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(B7/BB-1, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT Glycoproteins, specific or class
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(CAM, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT Antigens
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(CD2, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT Antigens
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(CD28, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT Antigens
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(CD44, **monoclonal antibodies** to adhesion mol. or T

cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Antigens

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(CD56, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Antigens

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(CD59, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Antigens

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(CDw52, CD52; **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Antigens

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(CTLA-4 (cytotoxic T-lymphocyte-activating, 4), sol. form or fusion protein contg.; **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Glycophosphoproteins

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(E-selectins, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Antigens

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(HML-1, CD103; **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Glycoproteins, specific or class

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(ICAM-1 (intercellular adhesion mol. 1), **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Glycoproteins, specific or class

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(ICAM-2 (intercellular adhesion mol. 2), **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Glycoproteins, specific or class

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

- (ICAM-3 (intercellular adhesion mol. 3), **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT Glycoproteins, specific or class
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(L-selectins, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT Lymphocyte
(T-cell, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT Antigens
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(Thy-1, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT Sialoglycoproteins
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(VCAM-1 (vascular cell adhesion mol. 1), **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(allo-, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT Integrins
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(antigens LFA-1, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT Adhesion
(bio-, inhibitor; **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT Intestine
(colon, **transplant**; **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fusion products, CTLA4-Ig; **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT Glycoproteins, specific or class
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(gp39, **monoclonal antibodies** to adhesion mol. or T

cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT **Transplant and Transplantation**

(**graft-vs.-host** reaction, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Lymphokines and Cytokines

RL: BSU (Biological study, unclassified); BIOL (Biological study) (interleukin 10, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Lymphokines and Cytokines

RL: BSU (Biological study, unclassified); BIOL (Biological study) (interleukin 12, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Lymphokines and Cytokines

RL: BSU (Biological study, unclassified); BIOL (Biological study) (interleukin 15, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Lymphokines and Cytokines

RL: BSU (Biological study, unclassified); BIOL (Biological study) (interleukin 1.alpha., **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Lymphokines and Cytokines

RL: BSU (Biological study, unclassified); BIOL (Biological study) (interleukin 1.beta., **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Lymphokine and cytokine receptors

Lymphokines and Cytokines
Receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (interleukin 2, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Lymphokines and Cytokines

RL: BSU (Biological study, unclassified); BIOL (Biological study) (interleukin 4, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Lymphokines and Cytokines

RL: BSU (Biological study, unclassified); BIOL (Biological study) (interleukin 6, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)

IT Lymphokines and Cytokines

RL: BSU (Biological study, unclassified); BIOL (Biological study) (interleukin 7, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for

- inhibiting **graft** vs. host disease in tissue or organ
transplant recipients)
- IT Lymphokines and Cytokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(interleukin 9, **monoclonal antibodies** to adhesion
mol. or T cell growth factor receptor or T cell signal costimulator for
inhibiting **graft** vs. host disease in tissue or organ
transplant recipients)
- IT Sialoglycoproteins
RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
unclassified); BIOL (Biological study)
(leukosialins, **monoclonal antibodies** to adhesion
mol. or T cell growth factor receptor or T cell signal costimulator for
inhibiting **graft** vs. host disease in tissue or organ
transplant recipients)
- IT **Antibodies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**monoclonal, monoclonal antibodies** to
adhesion mol. or T cell growth factor receptor or T cell signal
costimulator for inhibiting **graft** vs. host disease in tissue
or organ **transplant** recipients)
- IT Spleen
(splenocyte, **monoclonal antibodies** to adhesion mol.
or T cell growth factor receptor or T cell signal costimulator for
inhibiting **graft** vs. host disease in tissue or organ
transplant recipients)
- IT Bone marrow
Heart
Intestine
Kidney
Liver
Lung
Organ
Pancreatic islet of Langerhans
Skin
(**transplant, growth factor** receptor or T
cell signal costimulator for inhibiting **graft** vs.
host disease in tissue or
organ transplant recipientsHearty)
gROLES ASSIGNBiIntestineSESROLES
KidneyASROLES ASSIGNCTLiverstuROLES ASSIalROLES
ASSIGNED INTOrganLROLEPancreatic isle)
- IT *****Integrins**
RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
unclassified); BIOL (Biological study)
(.alpha.1.beta.1, **monoclonal antibodies** to adhesion
mol. or T cell growth factor receptor or T cell signal costimulator for
inhibiting **graft** vs. host disease in tissue or organ
transplant recipients)
- IT **Integrins**
RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
unclassified); BIOL (Biological study)
(.alpha.2.beta.1, **monoclonal antibodies** to adhesion
mol. or T cell growth factor receptor or T cell signal costimulator for
inhibiting **graft** vs. host disease in tissue or organ
transplant recipients)
- IT **Integrins**
RL: ADV (Adverse effect, including toxicity); BSU (Biological study,
unclassified); BIOL (Biological study)
(.alpha.3.beta.1, **monoclonal antibodies** to adhesion
mol. or T cell growth factor receptor or T cell signal costimulator for
inhibiting **graft** vs. host disease in tissue or organ
transplant recipients)

- IT **Integrins**
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.4.beta.1, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT **Integrins**
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.5.beta.1, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT **Integrins**
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.6.beta.1, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT **Integrins**
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(.beta.1, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT **Integrins**
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(.beta.3, **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT **Integrins**
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(.beta.4, CD104; **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- IT **Interferons**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.gamma., **monoclonal antibodies** to adhesion mol. or T cell growth factor receptor or T cell signal costimulator for inhibiting **graft** vs. host disease in tissue or organ **transplant** recipients)
- L65 ANSWER 36 OF 49 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:873806 HCAPLUS
DN 123:282535
TI Normalization of pancreatic exocrine enzymes by islet **transplantation** in diabetic rats
AU Lee, P. C.; Jordan, M.; Pieper, G. M.; Roza, A. M.
CS Dep. Gastroenterology, Pediatric, Pharmacology Toxicology, Med. Coll. Wisconsin, Milwaukee, WI, 53226, USA
SO Biochemistry and Cell Biology (1995), 73(5 & 6), 269-73
CODEN: BCBIEQ; ISSN: 0829-8211
PB National Research Council of Canada
DT Journal
LA English
CC 14-8 (Mammalian Pathological Biochemistry)

- AB In an effort to evaluate the effectiveness of islet **transplantation** in correcting exocrine dysfunction, young male Lewis rats were made diabetic b i.v. streptozotocin injection. Diabetes status was confirmed by decrease in **insulin** and increase in blood glucose and glycosylated Hb levels. Pancreatic islets were isolated from age-matched control syngeneic rats by collagenase digestion followed by purifn. through a Ficoll gradient. Islets (-1200) were **grafted** to the liver by intraportal injection to animals at 8 wk after diabetes was established. **Transplanted** rats were sacrificed 4 wk after correction of hyperglycemia. Diabetes resulted in decrease in body wt. **Transplantation** reversed the body wt. loss and led to a body wt. gain. Diabetes resulted in a decrease in pancreatic amylase (1.4 \pm 0.4 U/mg protein compared with a control value 121.9 \pm 3.2 U/mg protein) and a slight increase in lipase (87.3 \pm 5.5 U/mg protein compared with a control value of 69 \pm 4.7 U/mg protein). **Transplantation** completely normalized amylase (132.2 \pm 25.0 U/mg protein) and lipase (56.3 \pm 3.9 U/mg protein) in spite of an imperfect correction of blood **insulin**, glucose, and glycosylated Hb levels in these rats. These data demonstrated that islet **transplantation** is very effective in correcting the exocrine enzyme changes resulting from diabetes. Evaluation of steady-state levels of amylase mRNA in these groups of animals by Northern blots showed a decrease in the amylase mRNA level in diabetes and a return to that of control in **transplanted** rats, indicating that the control of amylase expression is most likely at the pretranslational level.
- ST lipase amylase islet **transplantation** diabetes mellitus
- IT Diabetes mellitus
Liver
Transcription, genetic
Transplant and Transplantation
(amylase, lipase and mRNA normalization by islet **transplantation** to liver in diabetic rat)
- IT Ribonucleic acids, messenger
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(amylase, lipase and mRNA normalization by islet **transplantation** to liver in diabetic rat)
- IT **Pancreatic islet of Langerhans**
(**transplant**, amylase, lipase and mRNA normalization by **islet transplantation** to liver in diabetic rat)
- IT 9000-92-4, Amylase **9001-62-1**, Lipase
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(amylase, lipase and mRNA normalization by islet **transplantation** to liver in diabetic rat)
- L65 ANSWER 37 OF 49 HCAPLUS COPYRIGHT 2002 ACS
- AN 1995:770139 HCAPLUS
- DN 123:254010
- TI Prolongation of rat islet **allograft** survival by treatment with **monoclonal antibodies** against VLA-4 and LFA-1
- AU Yang, Hua; Issekutz, Thomas B.; Wright, James R. Jr.
- CS Departments of Pathology, Izaak Walton Killam Children's Hospital, Halifax, NS, B3J 3G9, Can.
- SO Transplantation (1995), 60(1), 71-6
CODEN: TRPLAU; ISSN: 0041-1337
- PB Williams & Wilkins
- DT Journal
- LA English
- CC 15-3 (Immunochemistry)
- AB In this study, we investigated the effects of treatment with **monoclonal antibodies** against the VLA-4 and LFA-1 adhesion mols. on rat islet **allograft** rejection. TA-2 and TA-3

are function-blocking **mAb** against rat VLA-4 and LFA-1, resp. Lewis rats were made diabetic (plasma glucose levels > 22.2 mmol/L) with streptozotocin. One week later, 1500 freshly isolated Wistar Furth rat islets were **transplanted** under the left kidney capsule of each rat. **Monoclonal antibodies** were administered i.v. at a dosage of 2 mg on the day of islet **transplantation** and then i.p. every second day for 3 wk or until **graft** rejection. Plasma glucose levels were monitored at least 3 times a week and blood leukocyte counts were monitored every 4 days. Rejection was defined as 2 plasma glucose levels > 11.1 mmol/L. Mean **graft** survival times in untreated and control **mAb**-treated rats were 5.3 and 6.0 days, resp. Treatment with anti-VLA-4 or anti-LFA-1 resulted in only modest prolongation of mean **graft** survival time (9.3 and 7.4 days, resp.). However, treatment with the combination of anti-VLA-4 plus anti-LFA-1 resulted in long-term (i.e., 60-day) **graft** survival in 5 of 7 rats. **Graft** nephrectomy and histol. confirmed islet **graft** survival at 60 days. A second Wistar Furth rat islet **graft** under the opposite renal capsule after **graft** nephrectomy did not show full tolerance; however, the function of the second **graft** was significantly prolonged without any immunosuppression. Combined blockade of VLA-4 and LFA-1 also markedly prolonged islet **graft** survival when islets were **transplanted** via the portal vein. In conclusion, both VLA-4 and LFA-1 play a role in islet **allograft** rejection and blockade of both prevents or greatly delays **graft** rejection.

ST VLA4 LFA1 pancreatic islet **allograft** rejection;
monoclonal antibody VLA4 LFA1 pancreas **allograft**

IT **Pancreatic islet of Langerhans**
(allotransplant, treatment with monoclonal
antibodies against VLA-4 and LFA-1 prolongs rat pancreatic
islet **allograft** survival)

IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antigens LFA-1, treatment with monoclonal antibodies
against VLA-4 and LFA-1 prolongs rat pancreatic islet **allograft**
survival)

IT **Antibodies**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(monoclonal, treatment with monoclonal
antibodies against VLA-4 and LFA-1 prolongs rat pancreatic
islet **allograft** survival)

IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.4.beta.1, treatment with monoclonal
antibodies against VLA-4 and LFA-1 prolongs rat pancreatic
islet **allograft** survival)

L65 ANSWER 38 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 1995:627461 HCAPLUS

DN 123:110034

TI Immunomodulation of pancreatic islet **allografts** in mice with
CTLA4Ig secreting muscle cells

AU Chahine, A. Alfred; Yu, Ming; McKernan, Melissa M.; Stoeckert, Christian;
Lau, Henry T.

CS Children's Hospital of Philadelphia, University of Pennsylvania,
Philadelphia, 19104, USA

SO Transplantation (1995), 59(9), 1313-18
CODEN: TRPLAU; ISSN: 0041-1337

DT Journal

LA English

CC 15-10 (Immunochemistry)

AB In an effort to create a model of in vivo prodn. of immunosuppressants,

the authors have transfected C2C12 muscle cells (H-2k) with the cDNA for CTLA4Ig, a fusion protein that prevents the activation of T cells by blocking the costimulatory signal transduced by the T cell receptors CD28 and CTLA4. CTLA4Ig-secreting clones were **cotransplanted** with islets as composite **grafts** in the renal subcapsular space of diabetic mice. When the myoblasts were syngeneic to C3H/HeJ hosts (H-2k), there was a significant prolongation of survival of allogeneic C57BL/6J (H-2b) islets from a mean 11.0 days to 31.7 days. When the **graft** was completely allogeneic (H-2k myoblasts and islets into H-2b recipients), there was no benefit in survival. A transient blockade of LFA-1 with the **mAb** M17 was synergistic in this combination: 8 out of 12 C57BL/6J recipients achieved long-term acceptance. Systemic CTLA4Ig levels were detected up to 60 days after **transplantation**. In conclusion, the authors have shown that C2C12 muscle cells can be genetically engineered to secrete functional CTLA4Ig and that they can be used as a gene reservoir for the continuous in vivo prodn. of CTLA4Ig to modulate the survival of islet cell **allografts**.

- ST pancreas islet **allograft** CTLA4Ig protein muscle
- IT Immunosuppressants
 - (pancreatic islet **allograft** rejection is suppressed by **cotransplant** of syngeneic CTLA4Ig-secreting muscle cells)
- IT Diabetes mellitus
 - (suppression of pancreatic islet **allograft** rejection by **cotransplant** of syngeneic CTLA4Ig-secreting muscle cells)
- IT Antigens
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (CTLA-4 (cytotoxic T-lymphocyte-activating, 4), fusion products, with IgG2a .gamma. chain; suppression of pancreatic islet **allograft** rejection by **cotransplant** of syngeneic CTLA4Ig-secreting muscle cells)
- IT Immunoglobulins
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (G2a, fusion products, with CTLA4 proteins; suppression of pancreatic islet **allograft** rejection by **cotransplant** of syngeneic CTLA4Ig-secreting muscle cells)
- IT **Transplant and Transplantation**
 - (**allo-**, **pancreatic islet**; suppression of rejection by **cotransplant** of syngeneic CTLA4Ig-secreting muscle cells)
- IT **Pancreatic islet of Langerhans**
 - (**allotransplant**, suppression of rejection by **cotransplant** of syngeneic CTLA4Ig-secreting muscle cells)
- IT **Integrins**
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (antigens LFA-1, pancreatic islet **allograft** rejection is suppressed by **cotransplant** of CTLA4Ig-secreting muscle cells and administration of **monoclonal antibody** to)
- IT **Antibodies**
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (**monoclonal**, anti-LFA-1; pancreatic islet **allograft** rejection is suppressed by **cotransplant** of CTLA4Ig-secreting muscle cells and administration of)
- IT Muscle
 - (**transplant**, suppression of pancreatic islet **allograft** rejection by **cotransplant** of syngeneic CTLA4Ig-secreting muscle cells)

L65 ANSWER 39 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 1995:625530 HCAPLUS

DN 123:109727

TI Anti-ICAM-1/LFA-1 **monoclonal antibody** therapy prevents **graft** rejection and IDDM recurrence in BB rat pancreas **transplantation**

- AU Uchikoshi, F.; Ito, T.; Kamiike, W.; Moriguchi, A.; Nozaki, S.; Ito, A.;
Kuhara, A.; Miyata, M.; Matsuda, H.; et al.
- CS Medical School, Osaka University, Osaka, 565, Japan
- SO Transplantation Proceedings (1995), 27(2), 1527-8
CODEN: TRPPA8; ISSN: 0041-1345
- DT Journal
- LA English
- CC 15-3 (Immunochemistry)
- AB **Insulin**-dependent diabetes mellitus (IDDM) is generally considered to be induced by an autoimmune mechanism. From this point of view, pancreatic **grafts** in IDDM patients can be destroyed by the autoimmune mechanism as well as by an **allograft** rejection. Previously the recurrence was reported of IDDM in segmental pancreatic **grafts** from the identical twin or haplotype-identical sibling. To achieve long-term survival of pancreatic **grafts**, it is important to prevent IDDM recurrence in the **graft** as well as to control **graft** rejection. Spontaneously diabetic Biobreeding (BB) rats are well known as an animal model of human IDDM, and the etiol. of IDDM in these animals is reported to be very similar to that of human IDDM. Pancreas **transplantation** in BB rats may be a useful model for investigating the mechanisms of **graft** rejection and recurrence of IDDM. In this study, the authors examd. the efficacy of **monoclonal antibodies** against adhesion mols., such as ICAM-1 and LFA-1, in controlling **graft** rejection and preventing the recurrence of IDDM.
- ST ICAM1 antibody pancreas **transplant** diabetes therapy; LFA1 **integrin** antibody pancreas diabetes therapy
- IT Rat
(Biobreeding; **monoclonal antibodies** to ICAM-1/LFA-1 prevent pancreatic islet **allograft** rejection and recurrence of diabetes in)
- IT Glycoproteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ICAM-1 (intercellular adhesion mol. 1), **monoclonal antibodies** to ICAM-1/LFA-1 prevent pancreatic islet **allograft** rejection and recurrence of diabetes in Biobreeding rat)
- IT **Transplant and Transplantation**
(**allo-**, **pancreatic islet**; **monoclonal antibodies** to ICAM-1/LFA-1 prevent **graft** rejection and recurrence of diabetes in Biobreeding rat)
- IT **Pancreatic islet of Langerhans**
(**allotransplant**, **monoclonal antibodies** to ICAM-1/LFA-1 prevent **graft** rejection and recurrence of diabetes in Biobreeding rat)
- IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (antigens LFA-1, **monoclonal antibodies** to ICAM-1/LFA-1 prevent pancreatic islet **allograft** rejection and recurrence of diabetes in Biobreeding rat)
- IT Diabetes mellitus
(**insulin-dependent**, **monoclonal antibodies** to ICAM-1/LFA-1 prevent pancreatic islet **allograft** rejection and recurrence of diabetes in Biobreeding rat)
- IT **Antibodies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (**monoclonal**, anti-ICAM-1/LFA-1; prevention of pancreatic islet **allograft** rejection and recurrence of diabetes in Biobreeding rat by)

- TI In vitro and in vivo evaluation of protamine-**heparin** membrane for microencapsulation of rat **langerhans islets**
- AU Tatarkiewicz, Krystyna; Sitarek, Elzbieta; Fiedor, Piotr; Sabat, Marek; Orłowski, Tadeusz
- CS Institute Biocybernetics and Biomedical Engineering, Polish Academy Sciences, Warsaw, 02-109, Pol.
- SO Artificial Organs (1994), 18(10), 736-9
CODEN: ARORD7; ISSN: 0160-564X
- DT Journal
- LA English
- CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
- AB Rat pancreatic **islets** were microencapsulated with multilayer protamine-**heparin** (PH) membrane. Basal and stimulatory **insulin** secretion of microencapsulated **islets** was similar to the controlled free **islets** in vitro. During the long-term culture (up to 2 wk) mean **insulin** release of encapsulated **islets** did not significantly differ from the mean of free ones (the ratio of mentioned means was 54-167%). Empty PH microcapsules **transplanted** into Wistar rats i.p. and under the kidney capsule were generally harmless up to 4 mo. In only a few cases traces of fibrotic tissue around capsules entrapped in the omentum were found. No damage of microcapsules structure was obsd. The worst results were obtained in the instance of retroperitoneal **transplantation**. We conclude, therefore, that PH membrane was proved to be highly biocompatible, nontoxic for **islets**, and did not impair viability and glucose-dependent **insulin** secretion of **Langerhans islets** in in vitro culture.
- ST protamine **heparin** membrane microcapsule **langerhans islet**
- IT **Pancreatic islet of Langerhans**
(in vitro and in vivo evaluation of protamine-**heparin** membrane for microencapsulation of rat **langerhans islets**)
- IT Protamines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro and in vivo evaluation of protamine-**heparin** membrane for microencapsulation of rat **langerhans islets**)
- IT Pharmaceutical dosage forms
(microcapsules, in vitro and in vivo evaluation of protamine-**heparin** membrane for microencapsulation of rat **langerhans islets**)
- IT Protamines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sulfates, in vitro and in vivo evaluation of protamine-**heparin** membrane for microencapsulation of rat **langerhans islets**)
- IT 9002-98-6 9005-38-3, Sodium alginate 9005-49-6, **Heparin**, biological studies 10043-52-4, Calcium chloride, biological studies 26913-06-4, Poly[imino(1,2-ethanediyl)]
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro and in vivo evaluation of protamine-**heparin** membrane for microencapsulation of rat **langerhans islets**)
- L65 ANSWER 41 OF 49 HCAPLUS COPYRIGHT 2002 ACS
- AN 1994:678806 HCAPLUS
- DN 121:278806
- TI Inhibition of **transplant** rejection by pretreatment of xenogeneic pancreatic islet cells with anti-ICAM-1 antibodies
- AU Zeng, Yijun; Gage, Andrew; Montag, Anthony; Rothlein, Robert; Thistlethwaite, J. Richard; Bluestone, Jeffrey A.

CS Ben May Institute, University Chicago, Chicago, IL, USA
SO Transplantation (1994), 58(6), 681-9
CODEN: TRPLAU; ISSN: 0041-1337
DT Journal
LA English
CC 15-10 (Immunochemistry)
AB Cognate recognition of antigen-presenting cells by antigen-specific T cells is critically dependent on non-cognate adhesive interactions. For instance, several studies have shown that in vivo anti-LFA-1 plus anti-ICAM-1 mAb treatment results in prolongation of **allograft** survival. The authors have developed a xenogeneic islet **transplant** model to investigate the role of various adhesion interactions in the xenogeneic response and study the effect of pretreating donor tissue with immunosuppressive drugs. Pancreatic islet cells were pretreated in vitro with anti-human ICAM-1 mAb, **transplanted** under the renal capsule of diabetic B6 mice in the absence of systemic immunosuppression and examd. for long-term **xenograft** acceptance. The survival of human islets pretreated with anti-human ICAM-1 was significantly prolonged (MST = 53 days, with 40% of **grafts** surviving >100 days). In contrast, the survival of human islets pretreated with the control antibody was similar to those of non-treated islets (MST = 7 days). A massive lymphocyte infiltrate into control **xenografts** was obsd. at 5 days post-**transplant**. In contrast, a lymphocyte infiltrate did not appear in the anti-ICAM-1-treated islets for at least 11 days. Only **mAbs** specific for the LFA-1 binding epitope of ICAM-1 were found to inhibit a mixed islet/lymphocyte reaction in vitro and block **graft** rejection in vivo. However, **graft** prolongation is not accompanied by systemic tolerance. Mice **transplanted** simultaneously with human islet cells treated with control Ig (left kidney) or anti-ICAM-1 (right kidney) rejected the control islets but not anti-ICAM-1-treated islets. These results suggest that the LFA-1/ICAM-1 interaction is a crit. component for **xenograft** rejection and, more important, that pretreatment of islet tissue with anti-adhesion mol. antibodies can profoundly alter **graft** recognition and rejection in the absence of any systemic drug therapy. However, **graft** prolongation is not accompanied by systemic tolerance induction.
ST ICAM 1 glycoprotein pancreatic islet **xenotransplant**; antibody
IT ICAM pancreatic islet **xenotransplant**
IT Lymphocyte
(ICAM-1/LFA-1 system in cellular infiltration in human pancreatic islet **xenograft** rejection)
IT Glycoproteins, specific or class
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(ICAM-1 (intercellular adhesion mol. 1), in rejection of human pancreatic islet **xenograft**)
IT **Integrins**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(antigens LFA-1, in rejection of human pancreatic islet **xenograft**)
IT **Antibodies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**monoclonal**, RR1; human pancreatic islet **xenograft** survival prolongation by anti-ICAM-1)
IT **Transplant and Transplantation**
(**xeno-**, **pancreatic islet**; ICAM-1/LFA-1 system in rejection of human)
IT **Pancreatic islet of Langerhans**
(**xenotransplant**, ICAM-1/LFA-1 system in rejection of human)
L65 ANSWER 42 OF 49 HCAPLUS COPYRIGHT 2002 ACS
AN 1994:628323 HCAPLUS
DN 121:228323

TI Characterization of a **monoclonal antibody** recognizing
 an epitope designated as canine leukocyte-associated antigen

AU Yang, Wen-Chic; Esquenazi, Violet; Carreno, Manuel; Vallone, Teresa;
 Fuller, Laphalle; Roth, David; Nery, Jose; Burke, George; Miller, Joshua

CS Department Surgery, University Miami School Medicine, Miami, FL, 33101,
 USA

SO Transplantation (1994), 58(2), 233-40
 CODEN: TRPLAU; ISSN: 0041-1337

DT Journal

LA English

CC 15-3 (Immunochemistry)

AB An IgG1 **monoclonal antibody** (mAb),
 designated as 15F1.5, was generated against surface determinants of a dog
 peripheral blood-derived PHA-induced IL-2-dependent T cell line. It
 reacted with 65-80% of peripheral blood mononuclear cells (PBMCs), 90-95%
 of polymorphonuclear cells (PMNs), 65-70% of thymocytes, 85-95% of Thy-1
 pos. cells and 85-95% of IL-2-dependent T lymphoid cells in flow
 cytometry. It was nonreactive with peripheral blood red cells and
 platelets. It immunopptd. 95 and 150 Kd proteins derived from detergent
 solubilized lymphocyte membranes. Indirect immunofluorescent and
 immunoperoxidase staining of frozen tissue sections demonstrated pos.
 reactivity to cells in lymphoid but not nonlymphoid tissues. The 15F1.5
antibody was not directly mitogenic for PBMC's. It caused
 significant decrease in the lymphoproliferative response to T-dependent B
 cell mitogens, such as pokeweed mitogen (PWM) and staphage lysate (SPL),
 without significant effects on responses to the T cell mitogens,
 phytohemagglutinin (PHA), and Con A. The mixed lymphocyte culture (MLC)
 response and both the proliferative and effector arms of the cellmediated
 cytotoxicity reactions (CMC) were inhibited in a dose-dependent manner.
 The mAb also inhibited the auto- and allolymphoproliferative
 reactivity of mixed lymphocyte kidney or islet cell cultures (MLKC and
 MLIC), and the adhesion of T lymphoblasts and PMA-treated PMNs to
 endothelial cells. In vivo administration of the 15F1.5 (20 mg/day for 5
 days) caused an immediate and prolonged redn. in MLC responses, assocd.
 with cell binding of the mAb to PBMC and epitope modulation
 during the course of treatment, as indicated by flow cytometry. These
 results suggest that 15F1.5 is an immunomodulating **antibody**
 reacting with canine LFA-1. Thus, this mAb would be useful in
 studying the role of LFA-1/ICAM-1 in **graft** rejection as well as
 other inflammatory responses. It would also allow the use of an animal
 model to investigate the immunoregulatory effects of in vivo
 administration of anti-CD11/CD18 **antibodies** in organ/tissue
transplants.

ST dog LFA 1 antigen characterization; **monoclonal antibody**
 LFA 1 antigen dog

IT Inflammation
 (monoclonal antibody recognizing canine LFA-1
 antigen in)

IT Canis familiaris
 (monoclonal antibody recognizing canine LFA-1
 antigen prepn. and characterization)

IT Mitogens
 (monoclonal antibody recognizing canine LFA-1
 antigen reactivity with)

IT Immunoglobulins
 RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); ANST
 (Analytical study); BIOL (Biological study); PREP (Preparation); USES
 (Uses)
 (G1, monoclonal, monoclonal antibody
 recognizing canine LFA-1 antigen prepn. and characterization)

IT Lymphocyte
 (T-cell, monoclonal antibody recognizing canine
 LFA-1 antigen reactivity with)

IT **Integrins**
 RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
 (antigens LFA-1, **monoclonal antibody** recognizing canine LFA-1 antigen prepn. and characterization)

IT Thymus gland
 (thymocyte, **monoclonal antibody** recognizing canine LFA-1 antigen reactivity with)

IT Kidney
Pancreatic islet of Langerhans
 (**transplant, monoclonal antibody** recognizing canine LFA-1 antigen reactivity with)

L65 ANSWER 43 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 1994:549087 HCAPLUS

DN 121:149087

TI Methods for inducing long-term immunological non-responsiveness to **allografts**

IN Orosz, Charles G.; Ferguson, Ronald G.; Kincade, Paul W.

PA Ohio State University Research Foundation, USA; Oklahoma Medical Research Foundation

SO PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K039-395

CC 1-7 (Pharmacology)

Section cross-reference(s): 15

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9415639	A1	19940721	WO 1994-US391	19940112 <--
	W: FI, HU, JP, NO, PL, RU				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

PRAI US 1993-3981 19930115 <--

AB Methods are provided for inducing long-term non-responsiveness to an **allograft**, even in the absence of immunosuppressive agents. The methods include interfering with the interaction of VLA-4 of the **allograft** recipient and VCAM-1 of the **allograft**. This can be accomplished e.g. by administration of an **antibody** with the same effective specificity as **monoclonal antibody** M/K-2 (a rat IgG1 recognizing VCAM-1) for a time period and in an amt. sufficient to induce long-term non-responsiveness to the **allograft**. The effect of M/K-2 in mice with cardiac **allografts** is described.

ST **allograft** nonresponsiveness VLA4 VCAM1 interaction inhibitor;
monoclonal antibody VLA4 **allograft** nonresponsiveness

IT **Transplant and Transplantation**
 (cardiopulmonary, long-term immunol. non-responsiveness to, induction of, VLA-4/VCAM-1 interaction interference in)

IT Antibodies
 RL: BIOL (Biological study)
 (to VCAM-1, for inducing long-term immunol. non-responsiveness to **allografts**)

IT Sialoglycoproteins
 RL: BIOL (Biological study)
 (VCAM-1 (vascular cell adhesion mol. 1), VLA-4 interaction with, inhibition of, for inducing long-term immunol. non-responsiveness to **allografts**)

IT **Transplant and Transplantation**

(**allo-**, long-term immunol. non-responsiveness to, induction of, VLA-4/VCAM-1 interaction interference in)

IT **Antibodies**

RL: BIOL (Biological study)

(**monoclonal**, to VCAM-1, for inducing long-term immunol. non-responsiveness to **allografts**)

IT Bone marrow

Heart

Kidney

Liver

Lung

Muscle

Pancreatic islet of Langerhans

Skin

(**transplant**, long-term immunol. non-responsiveness to, induction of, VLA-4/VCAM-1 interaction interference in)

IT **Integrins**

RL: BIOL (Biological study)

(.alpha.4.beta.1, VCAM-1 interaction with, inhibition of, for inducing long-term immunol. non-responsiveness to **allografts**)

L65 ANSWER 44 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 1994:267794 HCAPLUS

DN 120:267794

TI A potential immunosuppressive effect of anti-lymphocyte function-associated antigen-1 **monoclonal antibody** on islet **transplantation**

AU Gotoh, Mitsukazu; Fukuzaki, Takayuki; Monden, Morito; Dono, Keizo; Kanai, Toshio; Yagita, Hideo; Okumura, Kou; Mori, Takesada

CS Med. Sch., Osaka Univ., Suita, 565, Japan

SO Transplantation (1994), 57(1), 123-6

CODEN: TRPLAU; ISSN: 0041-1337

DT Journal

LA English

CC 15-3 (Immunochemistry)

Section cross-reference(s): 1

AB The immunosuppressive potentials of **mAbs** to lymphocyte function-assocd. antigen-1 (LFA-1) and CD2 mols. were examd. in murine islet **transplantation**. Crude digested islets from BALB/c (H-2d) mice were **transplanted** into the renal subcapsular space of streptozotocin-induced diabetic C57BL/6 (H- 2b) mice. The rat **mAbs** of KBA (anti-LFA-1) and RM2-1 (anti-CD2) were given i.p. immediately after **transplantation** and on the first day after **grafting** at a dose of 0.1 mg/mouse/day. In non-treated animals, the islet **allografts** were acutely rejected with a mean survival time (MST) of 19.6 days. Control isotype-matched anti-CD18 treatment did not prolong the MST of 12.8 days. Anti-LFA-1 treatment alone produced indefinite survival in 5 of 10 recipients with MST of 72.2 days. Anti-CD2 treatment failed to do so, although MST was marginally prolonged to 32.8 days. When both **mAbs** were given together, addnl. benefit with anti-CD2 treatment was not obsd. (MST: 77.4 days). In spite of the unresponsiveness to islet **allografts**, the animals did not suffer from any severe infectious disease. Mice bearing long-term functioning islets rejected third-party skin **grafts** as well as islet donor strain skin **grafts**. The long-term surviving islet **allografts** were also rejected coincidentally. These results indicate that a perioperative short course of anti-LFA-1 **mAb** treatment can induce unresponsiveness to islet **allografts**, although it is not systemic, and that costimulatory signals through these adhesion mols. play a central role in inducing an immune response leading to rejection of the **allografted** islets.

ST LFA1 antigen **antibody** pancreatic islet **transplantation**
; immunosuppression islet **transplantation monoclonal**

antibody LFA1

IT Immunosuppression
(by **monoclonal antibody** to LFA-1 antigen, of pancreatic islet **transplant** rejection in diabetes model)

IT Immunosuppressants
(**monoclonal antibody** to LFA-1 antigen as, in pancreatic islet **transplant** model)

IT Diabetes mellitus
(pancreatic islet **transplant** in model of, rejection of, suppression of, by **monoclonal antibody** to LFA-1 antigen)

IT Immunoglobulins
RL: BIOL (Biological study)
(G2a, monoclonal, to LFA-1 antigen, immunosuppression of pancreatic islet **transplant** rejection in diabetes model by)

IT **Transplant and Transplantation**
(allo-, of **pancreatic islet**, rejection of, suppression of, by **monoclonal antibody** to LFA-1 antigen)

IT **Pancreatic islet of Langerhans**
(**allotransplant**, rejection of, suppression of, by **monoclonal antibody** to LFA-1 antigen)

IT **Integrins**
RL: BIOL (Biological study)
(antigens LFA-1, **monoclonal antibody** to, immunosuppression of pancreatic islet **transplant** rejection in diabetes model by)

L65 ANSWER 45 OF 49 HCAPLUS COPYRIGHT 2002 ACS

AN 1994:578 HCAPLUS

DN 120:578

TI **Graft** copolymers of polycationic species and water-soluble polymers for treatment of cells

IN Desai, Neil P.; Soon-Shiong, Patrick; Sandford, Paul A.; Heintz, Roswitha E.

PA Clover Consolidated, Ltd., Switz.

SO PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A01N001-02

ICS C12P001-00; C12N005-00

CC 1-7 (Pharmacology)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9318649	A1	19930930	WO 1993-US2609	19930322 <--
	W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, LU, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD				
	US 5578442	A	19961126	US 1992-856137	19920323 <--
	AU 9338163	A1	19931021	AU 1993-38163	19930322 <--
	US 5834556	A	19981110	US 1996-697885	19960829 <--
PRAI	US 1992-856137		19920323 <--		
	WO 1993-US2609		19930322 <--		
AB	Cells are rendered nonadhesive and/or nonimmunogenic by treatment with a cationic polymer onto which is grafted a water-sol. polymer. The cationic polymer may be PEI, polyallylamine, polyvinylpyridine, a cationic polysaccharide, or an amino acid homopolymer or random copolymer. The water-sol. polymer may be PEG, poly(vinyl alc.), poly(acrylic acid), polyacrylamide, PVP, etc. The graft copolymer may be removed				

- from the cells by treatment with an anionic species. The copolymer can also be used in cell preservation, liposome stabilization, etc. Thus, anchorage-dependent human fibroblasts treated with poly-L-lysine-**grafted** PEG showed no substrate adherence or aggregation in suspension, but good viability for >24 h and a smooth, spherical morphol.
- ST cell adhesion **graft** copolymer; immunogenicity cell **graft** copolymer
- IT Polyethers, biological studies
RL: BIOL (Biological study)
(-polyamines, **graft**, with water-sol. polymers, animal cell adhesion inhibition by)
- IT Adrenal gland
Pancreatic islet of Langerhans
Thyroid gland
(adhesion of cells of, inhibition of, by cationic polymer with **engrafted** water-sol. polymer)
- IT Animal cell
Fibroblast
(adhesion of, inhibition of, by cationic polymer with **engrafted** water-sol. polymer)
- IT Antigens
RL: BIOL (Biological study)
(animal cell function as, inhibition of, by cationic polymer with **engrafted** water-sol. polymer)
- IT Anions
Albumins, biological studies
RL: BIOL (Biological study)
(cationic polymer with **engrafted** water-sol. polymer removal from animal cells with)
- IT Nerve
(network of, on surface, formation of, cationic polymer with **engrafted** water-sol. polymer in mask for)
- IT **Transplant and Transplantation**
(of **pancreatic islet**, poly-L-lysine/PEG **graft** copolymer effect on)
- IT Liposome
(stabilization of, cationic polymer with **engrafted** water-sol. polymer for)
- IT Receptors
RL: BIOL (Biological study)
(vitronectin binding by, on fibroblast surface, poly-L-lysine/PEG **graft** copolymer inhibition of)
- IT Cell membrane
(water-sol. polymer assocn. with, **grafting** onto cationic polymer effect on)
- IT Polymers, biological studies
Polysaccharides, biological studies
RL: BIOL (Biological study)
(water-sol., **graft**, with cationic polymers, animal cell adhesion inhibition by)
- IT Lymphoblast
(T-cell, adhesion of, inhibition of, by cationic polymer with **engrafted** water-sol. polymer)
- IT Polyelectrolytes
(anionic, cationic polymer with **engrafted** water-sol. polymer removal from animal cells with)
- IT Adhesion
(bio-, of animal cells, inhibition of, by cationic polymer with **engrafted** water-sol. polymer)
- IT Polyelectrolytes
(cationic, water-sol. polymer-**engrafted**, animal cell adhesion inhibition by)
- IT Liver

- (hepatocyte, adhesion of, inhibition of, by cationic polymer with **engrafted** water-sol. polymer)
- IT Virus, animal
(human immunodeficiency, T-lymphoblast sensitive to, adhesion of, inhibition of, by cationic polymer with **engrafted** water-sol. polymer)
- IT Coating materials
(masking, cationic polymer with **engrafted** water-sol. polymer as, for neural network formation)
- IT Polyethers, biological studies
RL: BIOL (Biological study)
(polyamine-, **graft**, with water-sol. polymers, animal cell adhesion inhibition by)
- IT Polyamines
RL: BIOL (Biological study)
(polyether-, **graft**, with water-sol. polymers, animal cell adhesion inhibition by)
- IT Amino acids, polymers
RL: BIOL (Biological study)
(polymers, **graft**, with water-sol. polymers, animal cell adhesion inhibition by)
- IT Animal growth regulators
RL: BIOL (Biological study)
(vitronectins, binding of, to receptor on fibroblast surface, poly-L-lysine/PEG **graft** copolymer inhibition of)
- IT 51-61-6, Dopamine, biological studies
RL: BIOL (Biological study)
(adhesion of cells secreting, inhibition of, by cationic polymer with **engrafted** water-sol. polymer)
- IT 9000-07-1, Carrageenan 9000-69-5, Pectin 9004-34-6D, Cellulose, oxidized 9004-61-9, Hyaluronic acid 9005-32-7D, Alginic acid, salts **9005-49-6, Heparin** sulfate, biological studies
9007-28-7, Chondroitin sulfate
RL: BIOL (Biological study)
(cationic polymer with **engrafted** water-sol. polymer removal from animal cells with)
- IT 151754-91-5
RL: BIOL (Biological study)
(fibroblast adhesion inhibition by)

L65 ANSWER 46 OF 49 HCAPLUS COPYRIGHT 2002 ACS
AN 1993:552366 HCAPLUS .
DN 119:152366
TI Study on effects of exogenous somatostatin on endocrine and exocrine functions of segmental **autotransplanted** pancreas in man
AU Emoto, Takashi
CS Med. Sch., Osaka Univ., Suita, 565, Japan
SO Osaka Daigaku Igaku Zasshi (1993), 45(3), 213-24
CODEN: ODIZAK; ISSN: 0369-710X
DT Journal
LA Japanese
CC 2-5 (Mammalian Hormones)
AB In an attempt to clarify the effects of exogenous somatostatin on endocrine and exocrine function after segmental **autotransplantation** of the pancreas, a long-acting somatostatin analog (SMS201-995) was administered by s.c. injection to 6 patients on whom segmental **autotransplantation** of the pancreas had been performed following total pancreatectomy. Saline was injected s.c. as a control. Test meal (Ensure Liq.: 250 mL) was given 1 h after s.c. injection. Plasma levels of glucose (BS) and **insulin** (IRI), vol. of pancreatic juice (VOL), and bicarbonate output (BO), amylase output (AO) and lipase output (LO) of pancreatic juice were measured. During the basal period prior to ingestion, **insulin** secretion,

VOL, and AO were suppressed with 0.156, 0.625, 0.625 .mu.g/kg of exogenous somatostatin, resp., and BO and LO were suppressed with 2.5 .mu.g/kg compared with the injection of saline. During the 1st h after test meal, **insulin** secretion was suppressed with 0.15 .mu.g/kg of exogenous somatostatin, and VOL, BO, AO and LO were each suppressed with 0.625 .mu.g/kg. Thus, endocrine function of the **transplanted** pancreas may be inhibited by SMS201-995 more sensitively than exocrine function, in terms of dose-dependency.

ST somatostatin pancreas **transplantation** endocrine exocrine
 IT **Pancreatic islet of Langerhans**
 (hormone secretion by, after pancreas **autotransplantation** in human)
 IT Pancreatic juice
 (vol. of, after pancreas **autotransplantation**, somatostatin effect on, in humans)
 IT **Transplant and Transplantation**
 (**auto-**, of **pancreas**, endocrine and exocrine function of, somatostatin effect on, in humans)
 IT Pancreas
 (**autotransplant**, endocrine and exocrine function of, somatostatin effect on, in humans)
 IT 51110-01-1, Somatostatin
 RL: BIOL (Biological study)
 (endocrine and exocrine function of **autotransplanted** pancreas response to, in humans)
 IT 50-99-7, Glucose, biological studies 9004-10-8, Insulin, biological studies
 RL: BIOL (Biological study)
 (of blood plasma, after pancreas **autotransplantation**, somatostatin effect on, in humans)
 IT 71-52-3, Bicarbonate, biological studies 1393-25-5, Secretin 9000-92-4, Amylase 9001-62-1, Lipase 9011-97-6, CCK
 RL: BIOL (Biological study)
 (secretion of, by pancreas after **autotransplantation**, somatostatin effect on, in humans)

L65 ANSWER 47 OF 49 HCAPLUS COPYRIGHT 2002 ACS
 AN 1993:241013 'HCAPLUS
 DN 118:241013
 TI Antithrombogenic sulfated glycosaminoglycan conjugates with polymers
 IN **Larsson, Rolf**; Westberg, David; Formgren, Birgitta; Uhlin, Anders
 PA **Corline Systems AB, Swed.**
 SO PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K031-725
 ICS A61K047-48; A61L033-00; C08B037-10
 CC 63-7 (Pharmaceuticals)
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9305793	A1	19930401	WO 1992-SE672	19920925 <--
	W: AU, CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
	SE 9102798	A	19930327	SE 1991-2798	19910926 <--
	SE 470006	B	19931025		
	SE 470006	C	19940217		
	AU 9226646	A1	19930427	AU 1992-26646	19920925 <--
	JP 06510783	T2	19941201	JP 1992-505995	19920925 <--
	EP 658112	A1	19950621	EP 1992-920440	19920925 <--
	EP 658112	B1	20010711		

R: DE, FR, GB, IT
 US 5529986 A 19960625 US 1994-211224 19940325 <--
 PRAI SE 1991-2798 A 19910926 <--
 WO 1992-SE672 A 19920925 <--

AB Sulfated glycosaminoglycan conjugates with polymers are prepd. and used to make surfaces antithrombogenic. Heparin was coupled to N-succinimidyl-3-(2-pyridyldithio)-propionate and then conjugated to intraocular lenses made of poly(Me methacrylate). The surface-heparinized lenses were incubated in human citrated whole blood for 60min and the lenses were then washed. Platelet adhesion to the heparinized lenses was reduced by 98% as compared with the untreated control lenses.

ST antithrombogenic glycosaminoglycan sulfate conjugate polymer; intraocular lens heparin polymethacrylate conjugate

IT Polymers, compounds
 RL: BIOL (Biological study)
 (aliph., conjugates, with sulfated glycosaminoglycans, antithrombogenic activity of)

IT Medical goods
 (antithrombogenic, surface treatment of, with antithrombogenic sulfated glycosaminoglycan conjugates)

IT Polysaccharides, compounds
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (conjugates, with sulfated glycosaminoglycan, antithrombogenic activity of)

IT Lenses
 (intraocular, surface treatment of, with antithrombogenic sulfated glycosaminoglycan conjugates)

IT Imines
 RL: BIOL (Biological study)
 (poly-, conjugates, with sulfated glycosaminoglycans, antithrombogenic activity of)

IT Glycosaminoglycans, compounds
 RL: BIOL (Biological study)
 (sulfated, conjugates, with polymer, antithrombogenic activity of)

IT 9011-14-7, Poly(methyl methacrylate)
 RL: BIOL (Biological study)
 (intraocular lenses manufd. with, surface treatment of, with antithrombogenic sulfated glycosaminoglycan conjugates)

IT 9002-13-5DP, Urease, conjugates with polylysine and heparin 9002-98-6DP, conjugates with sulfated glycosaminoglycans 9005-49-6DP, Heparin, polymer conjugates 9012-76-4DP, Chitosan, conjugates with sulfated glycosaminoglycans 24937-49-3P 25104-12-5DP, conjugates with sulfated glycosaminoglycans 25104-18-1DP, Polylysine, conjugates with sulfated glycosaminoglycans 30551-89-4DP, Polyallylamine, conjugates with sulfated glycosaminoglycans 38000-06-5DP, Polylysine, conjugates with sulfated glycosaminoglycans 71550-12-4DP, Polyallylamine hydrochloride, conjugates with sulfated glycosaminoglycans
 RL: PREP (Preparation)
 (prepn. of, as antithrombogenic medical agents)

IT 9002-88-4, Polyethylene
 RL: BIOL (Biological study)
 (tubing, surface treatment of, with antithrombogenic sulfated glycosaminoglycan conjugates)

L65 ANSWER 48 OF 49 HCAPLUS COPYRIGHT 2002 ACS
 AN 1993:198264 HCAPLUS
 DN 118:198264
 TI Method for manufacturing a protein membrane for encapsulating biological and/or biologically active materials
 IN Tatarkiewicz, Krystyna
 PA Polska Akademia Nauk, Instytut Biocybernetyki i Inżynierii Biomedycznej, Pol.

SO Pol., 2 pp.
 CODEN: POXXA7
 DT Patent
 LA Polish
 IC ICM C12N005-00
 ICS A61K009-52
 CC 63-7 (Pharmaceuticals)
 Section cross-reference(s): 14
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	PL 154373	B1	19910830	PL 1987-267078	19870730 <--
AB	An artificial membrane can be prepd. which is suitable for encapsulating biol. active materials or cells or tissue fragments for transplantation into the body. Thus, drops of 1.2% aq. soln. of Na alginate contg. pancreatic islets were added to a 1.5% soln. of CaCl ₂ in H ₂ O, whereby gelatinous spherules were formed. Then the supernatant was removed from the spherules and replaced with a 0.2% soln. of polyethylenimine. After 2 min the microcapsules were rinsed with a 1% soln. of CaCl ₂ , water, and physiol. saline buffered to pH 7.4. In succession, they were transferred to a bath contg. 0.1% protamine sulfate for 3 min, then the microcapsules were immersed in a heparin soln. (100 IU heparin /1 mg protamine). After 3 min. the microcapsules were washed repeatedly in physiol. saline at pH 7.4.				
ST	pancreas islet transplant membrane microcapsule; alginate protamine pancreas islet microcapsule				
IT	Encapsulation (of cells for transplantation , protein membrane for, prepn. of)				
IT	Transplant and Transplantation (of pancreatic islet , protein membrane for encapsulation of, prepn. of)				
IT	Membrane, biological (prepn. of proteinaceous, for encapsulating biol. active substances and cells for transplantation)				
IT	Pharmaceutical dosage forms (microcapsules, of cells, for transplantation , protein membrane for, prepn. of)				
IT	Protamines RL: BIOL (Biological study) (sulfates, in prepn. of membrane for encapsulating biol. active substances and cells for transplantation)				
IT	Pancreatic islet of Langerhans (transplant , protein membrane for encapsulation of, prepn. of)				
IT	9005-38-3, Sodium alginate RL: BIOL (Biological study) (in prepn. of membrane for encapsulating biol. active substances and cells for transplantation)				

L65 ANSWER 49 OF 49 HCAPLUS COPYRIGHT 2002 ACS
 AN 1991:575423 HCAPLUS
 DN 115:175423
 TI Persistent restoration of endogenous **insulin** production in animals with **insulin**-dependent diabetes
 AU Kudryashov, B. A.; Ul'yanov, A. M.
 CS Lab. Physiol. Biochem. Blood Coagulation, M. V. Lomonosov State Univ., Moscow, USSR
 SO Voprosy Meditsinskoi Khimii (1991), 37(4), 40-3
 CODEN: VMDKAM; ISSN: 0042-8809
 DT Journal
 LA Russian
 CC 2-6 (Mammalian Hormones)

AB Implantation of allogenic .beta.-cells into animals with alloxan diabetes did not produce a persistent pos. effect. The implanted .beta.-cells lost their viability as a result of the toxic effect of a natural diabetogenic factor occurring in blood plasma during **insulin**-dependent diabetes. Long-term administration of **heparin** to these animals within the first 90 days of the expt. prevented the neg. phenomenon and to neutralize the diabetogenic factor activity. Under these conditions the implanted .beta.-cells effectively produced endogenous **insulin** and the symptoms of diabetes disappeared within 14 mo.

ST **insulin beta cell transplant diabetes heparin**

IT Blood plasma
(diabetogenic factor of, in diabetes, **heparin** effect on)

IT **Transplant and Transplantation, animal**
(of **pancreatic islet .beta.-cells**, survival of, in diabetes, **heparin** increase of)

IT Diabetes mellitus
(pancreatic islet .beta.-cell **transplant** survival in, **heparin** increase of)

IT **Pancreatic islet of Langerhans**
(**transplant**, survival of, in diabetes, **heparin** effect on)

IT **9004-10-8, Insulin**, biological studies
RL: FORM (Formation, nonpreparative)
(formation of, by .beta.-cell **transplants** in diabetes, **heparin** effect on)

IT 103333-90-0, Diabetogenic factor
RL: BIOL (Biological study)
(of blood plasma, in diabetes, .beta.-cell **transplant** survival inhibition by, **heparin** attenuation of)

IT **9005-49-6, Heparin**, biological studies
RL: BIOL (Biological study)
(pancreatic islet .beta.-cell **transplant** survival increase by, in diabetes)

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FILE 'REGISTRY' ENTERED AT 11:31:34 ON 18 DEC 2002

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STRUCTURE FILE UPDATES: 17 DEC 2002 HIGHEST RN 476608-54-5

DICTIONARY FILE UPDATES: 17 DEC 2002 HIGHEST RN 476608-54-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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L68 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2002 ACS
RN 9005-49-6 REGISTRY

CN **Heparin (8CI, 9CI)** (CA INDEX NAME)

OTHER NAMES:

CN .alpha.-Heparin
CN Bemiparin
CN Certoparin
CN Clexane
CN Clivarin
CN Clivarine
CN CY 216
CN CY 222
CN Dalteparin
CN Enoxaparin
CN Fluxum
CN FR 860
CN Fragmin A
CN Fragmin B
CN Fraxiparin
CN Heparin subcutan
CN Heparin sulfate
CN Heparinic acid
CN KB 101
CN Multiparin
CN Novoheparin
CN OP 386
CN OP 622
CN Pabyrn
CN Parnaparin
CN Parvoparin
CN Reviparin
CN Sandoparin
CN Sublingula
CN Tinzaparin
CN Vetren
CN Vitrum AB
DR 9075-96-1, 11078-24-3, 11129-39-8, 104521-37-1, 37324-73-5, 91449-79-5
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyester, Polyester formed
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,
CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST,
CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES,
EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS,
NAPRALERT, NIOSHTIC, PHAR, PHARMASEARCH, PIRA, PROMT, RTECS*, TOXCENTER,
USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

19622 REFERENCES IN FILE CA (1962 TO DATE)

1862 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

19655 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:375368

REFERENCE 2: 137:375271

REFERENCE 3: 137:370345

REFERENCE 4: 137:367979

REFERENCE 5: 137:365538

REFERENCE 6: 137:365455
REFERENCE 7: 137:365406
REFERENCE 8: 137:363702
REFERENCE 9: 137:363700
REFERENCE 10: 137:363407

L68 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2002 ACS

RN 9004-10-8 REGISTRY

CN Insulin (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Actrapid

CN Actrapid HM

CN Actrapid MC

CN Decurvon

CN Dermulin

CN Endopancrine

CN Exubera

CN HMR 4006

CN Iletin

CN Insular

CN Insulin Injection

CN Insulyl

CN Intesulin B

CN Iszilin

CN Musulin

DR 8049-67-0, 8049-95-4, 9004-12-0, 9045-63-0, 9045-65-2, 9045-66-3,
9045-67-4, 9066-39-1, 9066-40-4, 11081-38-2, 57126-42-8, 37243-75-7,
37294-43-2, 69090-47-7, 88026-11-3, 88026-12-4

MF Unspecified

CI PMS, COM, MAN

PCT Manual registration

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,
CA, CABA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM,
CSNB, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA,
MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PDLCOM*, PHAR, PHARMASEARCH, PIRA,
PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL, VTB
(*File contains numerically searchable property data)

Other Sources: EINECS**, WHO

(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

81573 REFERENCES IN FILE CA (1962 TO DATE)

1493 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

81593 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:375275
REFERENCE 2: 137:375234
REFERENCE 3: 137:375159
REFERENCE 4: 137:375137
REFERENCE 5: 137:370080
REFERENCE 6: 137:369295
REFERENCE 7: 137:369293

REFERENCE 8: 137:369288

REFERENCE 9: 137:369266

REFERENCE 10: 137:369259

L68 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2002 ACS

RN 9000-94-6 REGISTRY

CN Antithrombin (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Antithrombin III

CN Heparin cofactor

CN Heparin cofactor B

CN Org 10849

CN Thrombin inhibitor

AR 90170-80-2

DR 9041-91-2, 52014-67-2

MF Unspecified

CI PMS, COM, MAN

PCT Manual registration

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,
CA, CANCERLIT, CAPLUS, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU,
DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT,
IFIUDB, IPA, MEDLINE, MSDS-OHS, NIOSHTIC, PHAR, PHARMASEARCH, PROMT,
RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL

(*File contains numerically searchable property data)

Other Sources: EINECS**

(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

4758 REFERENCES IN FILE CA (1962 TO DATE)

504 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

4765 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:369288

REFERENCE 2: 137:367979

REFERENCE 3: 137:367705

REFERENCE 4: 137:365455

REFERENCE 5: 137:365406

REFERENCE 6: 137:362854

REFERENCE 7: 137:350511

REFERENCE 8: 137:348831

REFERENCE 9: 137:348353

REFERENCE 10: 137:346941

=> d his

(FILE 'HOME' ENTERED AT 10:31:27 ON 18 DEC 2002)

SET COST OFF

FILE 'REGISTRY' ENTERED AT 10:31:38 ON 18 DEC 2002

E HEPARIN/CN

L1

1 S E3

L2 707 S HEPARIN
 L3 706 S L2 NOT L1
 E RGD/CN
 E THROMBIN/CN
 L4 1 S E3
 E ANTITHROMBIN/CN
 L5 1 S E3
 E INSULIN/CN
 L6 1 S E3
 L7 6380 S INSULIN
 L8 6379 S L7 NOT L6

FILE 'HCAPLUS' ENTERED AT 10:34:24 ON 18 DEC 2002

 E LANGERHAN/CT
 E E6+ALL
 E ILSET/CT
 E ILSET/CW
 L9 17621 S LANGERHAN?(L) ISLET
 E PANCREATIC ISLET/CT
 L10 15978 S E6-E31
 E E36+ALL
 L11 349 S E1
 E E2+ALL
 L12 15978 S E10
 L13 17621 S L9-L12
 L14 1819 S L13 AND ?TRANSPLANT?
 L15 920 S L13 AND ?GRAFT?
 E TRANSPLANT/CT
 L16 7190 S E3,E6-E24
 L17 8967 S E25-E36
 L18 8115 S E37-E48
 L19 4874 S E49-E60
 L20 5088 S E61-E67
 L21 1 S E68
 L22 494 S E72
 L23 811 S E73
 L24 811 S E76
 L25 1565 S E71
 E E5+ALL
 L26 29350 S E7-E12,E6+NT
 E E38+ALL
 L27 4404 S E2
 L28 1423 S L13 AND L16-L27
 L29 1871 S L14,L15,L28
 L30 20 S L29 AND L1
 L31 23 S L29 AND L3
 L32 22 S L29 AND HEPARIN
 L33 4 S L29 AND RGD
 L34 1 S L29 AND (ARG OR ARGIN?) () (GLY OR GLYC?) () (ASP OR ASPART?)
 E RGD/CT
 E E7+ALL
 L35 1 S L29 AND E3,E2
 L36 0 S L29 AND ARGINYLGLYCYLASEPART?
 L37 146 S L29 AND (MAB OR MONOCLON?(L)ANTIBOD?)
 L38 13 S L37 AND INTEGRIN
 E FC RECEPTOR/CT
 E E4+ALL
 E E2+ALL
 L39 5 S L37 AND E10-E12,E9+NT
 E E89+ALL
 L40 30 S L37 AND E7,E6+NT
 L41 3 S L39,L40 AND FC?
 L42 4 S L37 AND FC?

L43 1 S L29 AND (L4 OR THROMBIN OR FACTOR IIA) (L) (L5 OR ANTITHROMBIN
L44 655 S L29 AND L6
L45 88 S L29 AND L8
L46 1045 S L29 AND INSULIN
L47 1054 S L44-L46
L48 57 S L30-L35, L38, L39, L41, L42, L43
L49 31 S L48 AND L47
L50 57 S L48, L49
E KORSGREN O/AU
L51 54 S E3, E4
E KOERSGREN O/AU
E KOERSGEN O/AU
E KEORSGREN O/AU
E BENNET W/AU
L52 57 S E3-E13
E NILSSON B/AU
L53 488 S E3-E16
E NILSSON BO/AU
L54 209 S E3-E11
E LARSSON R/AU
L55 143 S E3, E4
E LARSSON ROLF/AU
L56 95 S E3, E4
L57 4 S L51-L56 AND L50
E CORLINE/PA, CS
L58 2 S E3-E6
L59 5 S L57, L58 AND L9-L58
E ANTICOAGULANT/CT
L60 12531 S E10, E12
E E12+ALL
E E2+ALL
L61 12884 S E4+NT
L62 7 S L60, L61 AND L29
L63 60 S L50, L62, L59
L64 49 S L63 AND (PD<=20000204 OR PRD<=20000204 OR AD<=20000204)
L65 49 S L59, L64
L66 11 S L63 NOT L65

FILE 'HCAPLUS' ENTERED AT 11:10:54 ON 18 DEC 2002
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FILE 'REGISTRY' ENTERED AT 11:27:50 ON 18 DEC 2002
L67 12 S E1-E12
L68 3 S L1, L4-L6 AND L67

FILE 'REGISTRY' ENTERED AT 11:31:34 ON 18 DEC 2002